Linfoma mantellare: terapia del paziente anziano

Francesco Zaja
Trieste

Dramatic demographic changes

- Increasing proportion of elderly persons
- In 2015 **19%** of the population in the European Union were ≥ 65 years old
  - 70–74 years: 4.4%
  - 75–79 years: 3.8%
  - ≥ 80 years: 5.3%
- By 2060 **28%** of the population will be ≥ 65 years
- ≥ 80 years old will rise to 12%
- Treatment options has increased dramatically over the past years

http://ec.europa.eu/eurostat/documents/2995521/7672228/3-29092016-AP-EN.pdf/4b90f6bb-43c1-45ed-985bdfbe9564157a

http://europa.eu/epc/sites/epc/files/docs/pages/ageing_report_2015_en.pdf

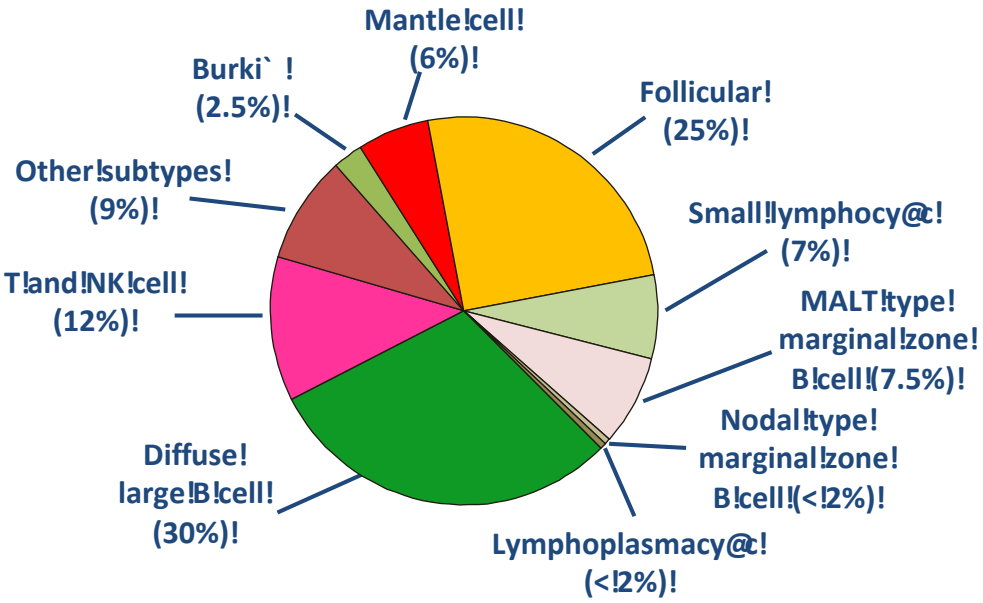
Assessing fitness in elderly patients with malignant lymphoma

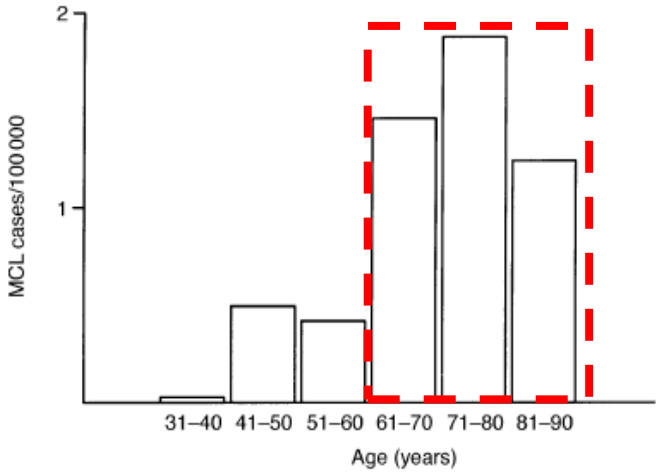
- Increase age is associated with increase TRM
- TRM in those aged 50–64 years: 4%
- TRM in those aged 75–79 years: 20% (when no antibacterial or antiviral prophylaxis was given)
- Geriatric assessment should be included

ESMO guidelines 2017

MCL: a rare lymphoma mainly of the elderly

Median age at diagnosis ~65





Andersen et al 2002, Danish Population Study

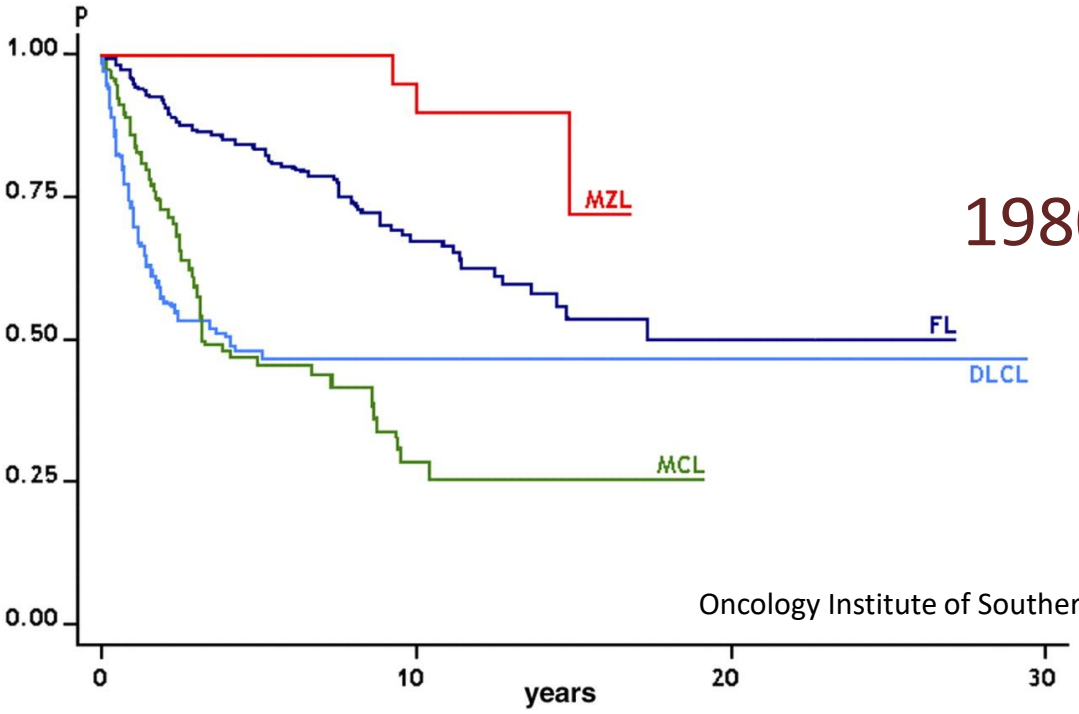
Ann Arbor stage	
I	84 (6.1)
II	108 (7.8)
III	167 (12.0)
IV	985 (70.9)

…and widespread at diagnosis

Lichtman. Williams Hematology, 7˚ Edition. 2006; 1408.

Abrahamsson et al 2014: Swedish-Danish Population Study

Cause-specific survival of the main B-cell lymphoma subtypes



1980-2006

Oncology Institute of Southern Switzerland, Ghielmini and Zucca, Blood 2009

Significant improvement in OS in the last 10 years:

1) *introduction of dose-intensive strategies upfront in younger patients*
2) *availability of novel agents in older patients or in the r/r setting.*

Valutazione Geriatrica Multidimensionale:

“FIT”	“UNFIT”	“FRAGILE”
• Non UNFIT • Non fragile	• Età > 80 • Criteri clinici-funzionali in base a specifici parametri	• Età > 80 • Criteri clinici-funzionali in base a specifici parametri
Standard	Terapia personalizzata	Terapia palliativa

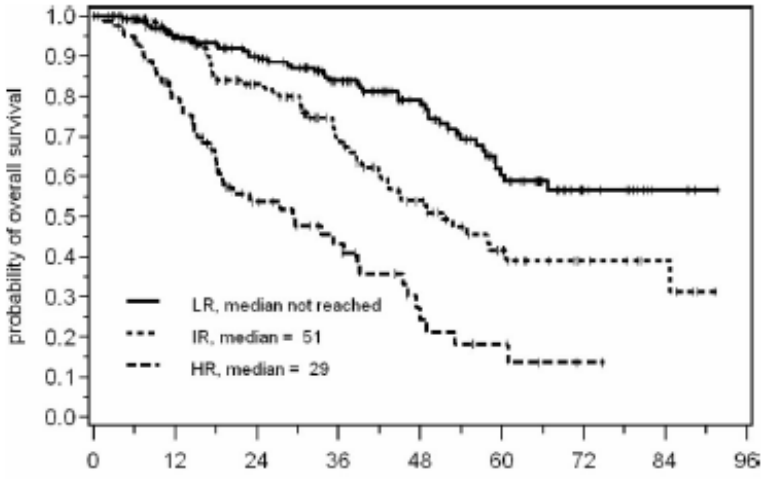
MIPI Index: historical data

Age x 0.03535)

+ 0.6978 (if **ECOG** >1)

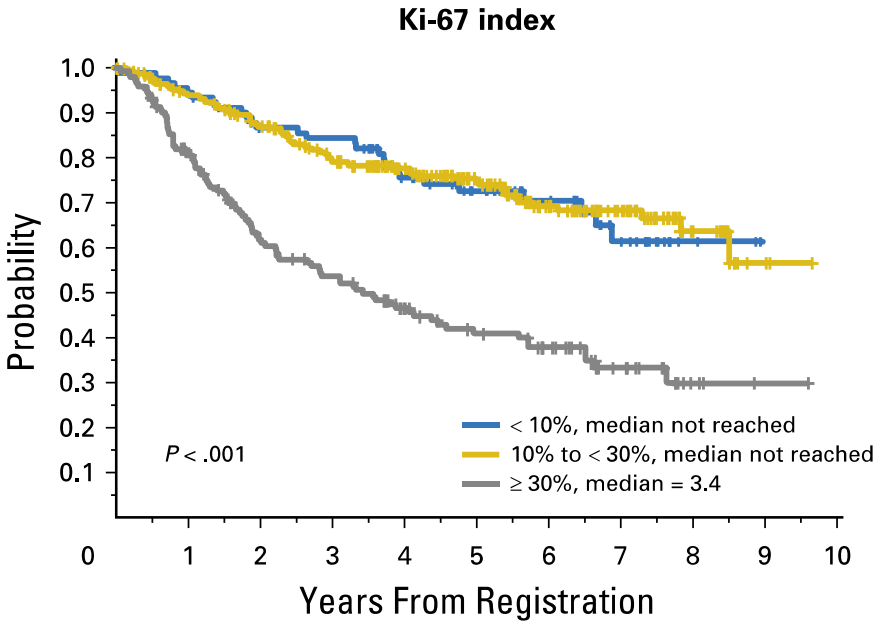
+ [1.367 x log10(**LDH**/ULN)]

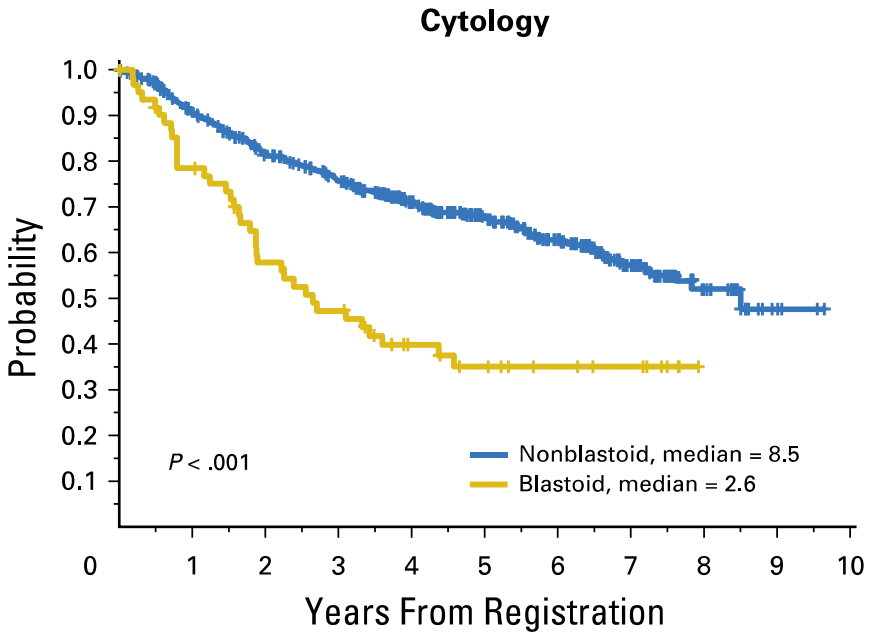
+ [0.9393 x log10(**WBC** count)]

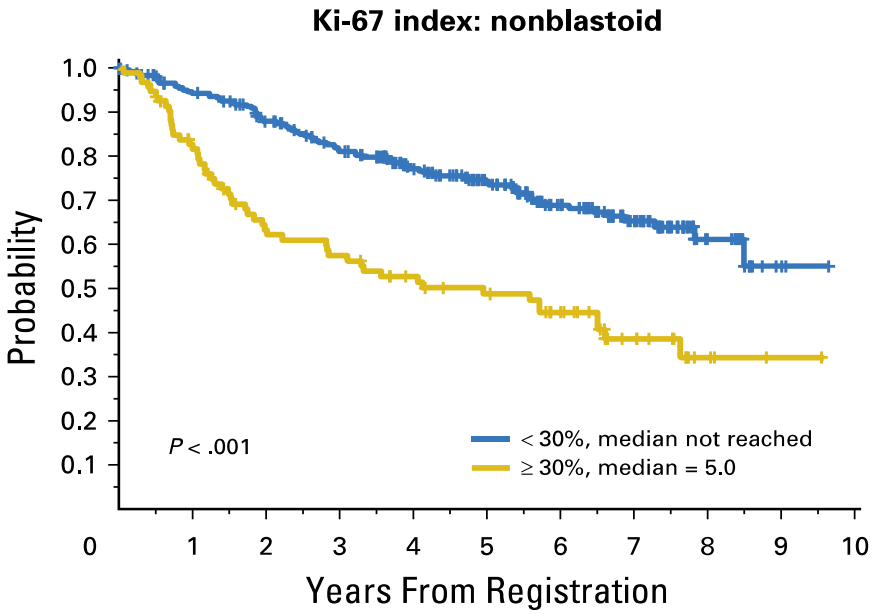


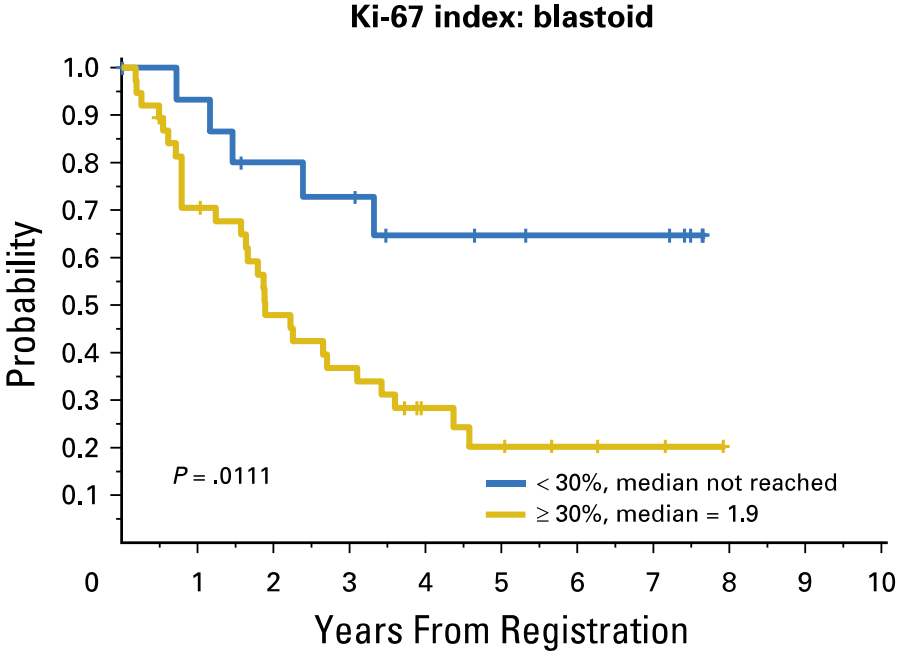
	Score	Patients (%)	Median OS (months)	5-years OS (%)
Low	< 5.7	44	NR	60
Intermediate	5.7-6.2	35	51	40
High	> 6.2	21	29	15

Hoster et al, Blood 2008









Hoster et al, JCO 2016

The Oncologist®

Hematologic Malignancies

Frontline Treatment for Older Patients with Mantle Cell Lymphoma

Haige Ye,[a,b,†] Aakash Desai,[b,c,†] Dongfeng Zeng,[b] Jorge Romaguera,[b] Michael L. Wang[b]

[a]Department of Hematology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China; [b]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [c]The University of Texas Health Science Center, Houston, Texas, USA

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 29: 544–562, 2018
doi:10.1093/annonc/mdx413
Published online 29 November 2017

SPECIAL ARTICLE

ESMO Consensus Conference on malignant lymphoma: general perspectives and recommendations for the clinical management of the elderly patient with malignant lymphoma

C. Buske[1*], M. Hutchings[2], M. Ladetto[3], V. Goede[4], U. Mey[5], P. Soubeyran[6], M. Spina[7], R. Stauder[8], M. Trněný[9], U. Wedding[10], P. Fields[11] & The ESMO Lymphoma Consensus Conference Panel Members[†]

Come trattare in 1L un paziente anziano con MCL ?

- Intermediate or high MIPI-c
- Tumor diameter ≥ 3 cm
- ↑ LDH or β-2M
- B symptoms
- Blastoid/pleomorphic variants
- Ki-67 > 30%
- Mutation of TP53, NOTCH1/2, MYC
- Indolent SOX-11 negative presentation

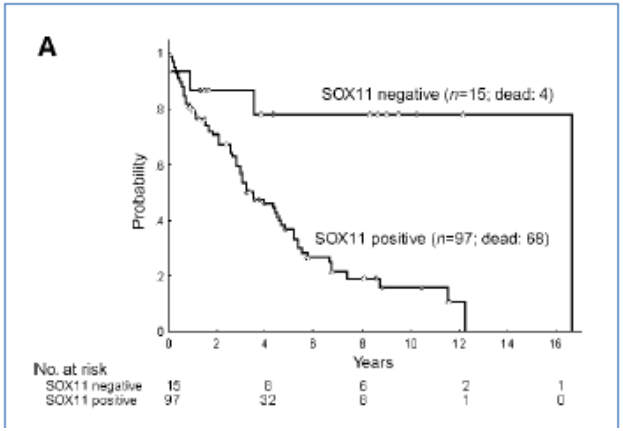
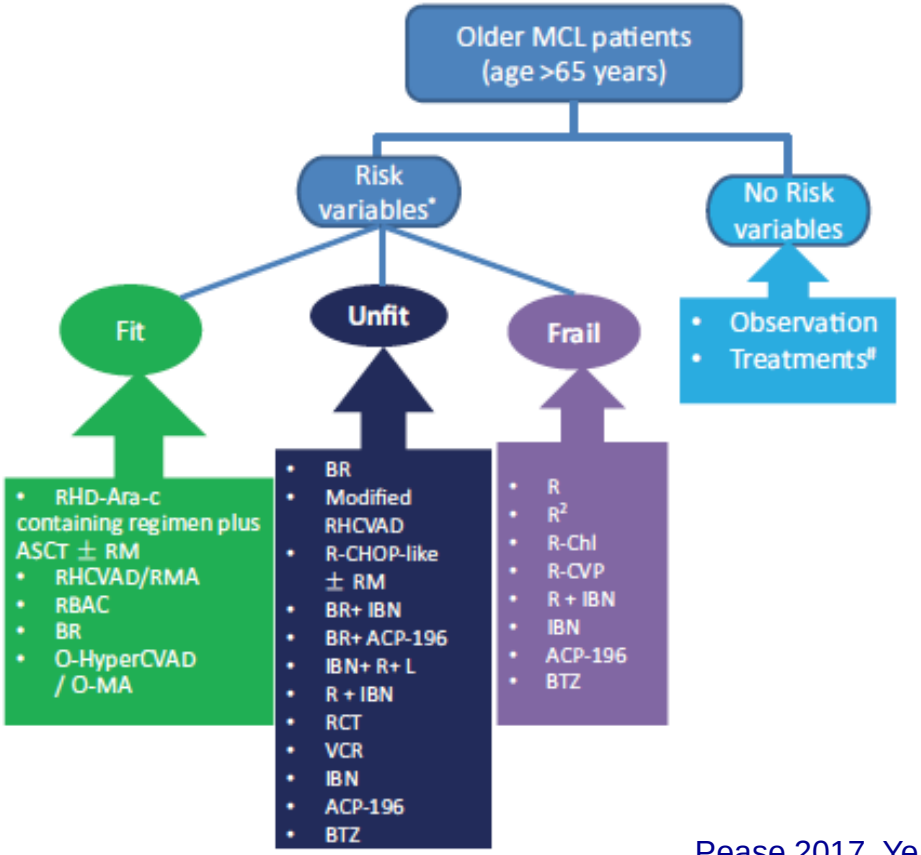


Table 1
Factors supporting initial observation of mantle cell lymphoma.[a]

Clinical	Asymptomatic Low tumor burden Normal LDH Normal β_2-microglobulin
Pathologic	Non-blastoid or pleomorphic morphology Ki-67 < 30%



Pease 2017, Ye et al. 2018

Come trattare in 1L un paziente anziano con MCL ?

The Oncologist®

Hematologic Malignancies

Frontline Treatment for Older Patients with Mantle Cell Lymphoma

HAIGE YE,[a,b,†] AAKASH DESAI,[b,c,†] DONGFENG ZENG,[b] JORGE ROMAGUERA,[b] MICHAEL L. WANG[b]

[a]Department of Hematology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, People's Republic of China; [b]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [c]The University of Texas Health Science Center, Houston, Texas, USA

"Thus, our recommendation is to use RHD-Ara-c containing regimen plus ASCT as frontline therapy in elderly fit patients".

Ye et al. 2018

R-HypercVAD/MA

- 8-year TTF: 16%
- 8-year OS: 33%
- 29% did not finished the planned program for toxicity
- **Not reccomended for patients > 65 years**

Autologous SCT in elderly MCL patients

- EBMT registry
- retrospectively study
- ASCT between 2000 and 2007
- **712 cases**
  - **79 cases > 65 years**
  - 633 cases < 65 years
- no differences in engraftment of neutrophils (12 vs. 12 days) and platelets (13 vs. 13 days)
- relapse rate (66% vs. 55%)
- 5-year PFS (29% vs. 40%)
- 5-year OS (61% vs. 67%)

Jantunen et al. Ann Oncol 2012

Autologous SCT in elderly MCL patients

- NRM at 3 months and 5 years after transplantation in > 65 years was not higher
- no special toxicity of the patients older than 65 with consolidation SCT
- ASCT can be performed in selected patients older than 65 years.

Jantunen et al. Ann Oncol 2012

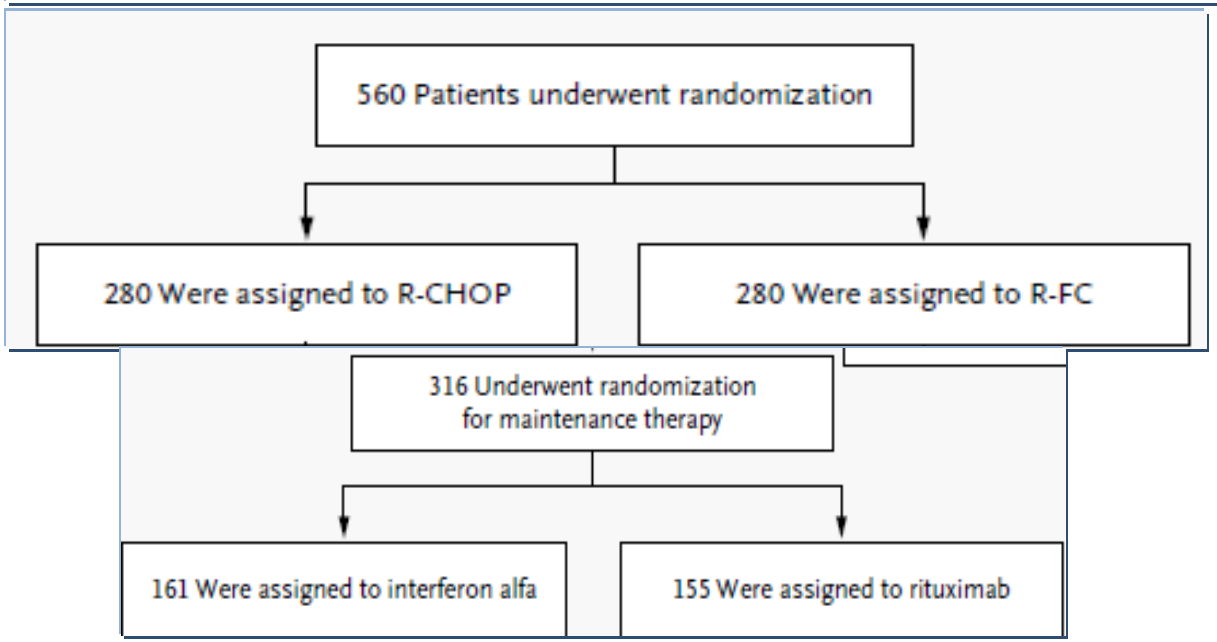
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Older Patients with Mantle-Cell Lymphoma

H.C. Kluin-Nelemans, E. Hoster, O. Hermine, J. Walewski, M. Trneny, C.H. Geisler, S. Stilgenbauer, C. Thieblemont, U. Vehling-Kaiser, J.K. Doorduijn, B. Coiffier, R. Forstpointner, H. Tilly, L. Kanz, P. Feugier, M. Szymczyk, M. Hallek, S. Kremers, G. Lepeu, L. Sanhes, J.M. Zijlstra, R. Bouabdallah, P.J. Lugtenburg, M. Macro, M. Pfreundschuh, V. Procházka, F. Di Raimondo, V. Ribrag, M. Uppenkamp, M. André, W. Klapper, W. Hiddemann, M. Unterhalt, and M.H. Dreyling

≥60 years



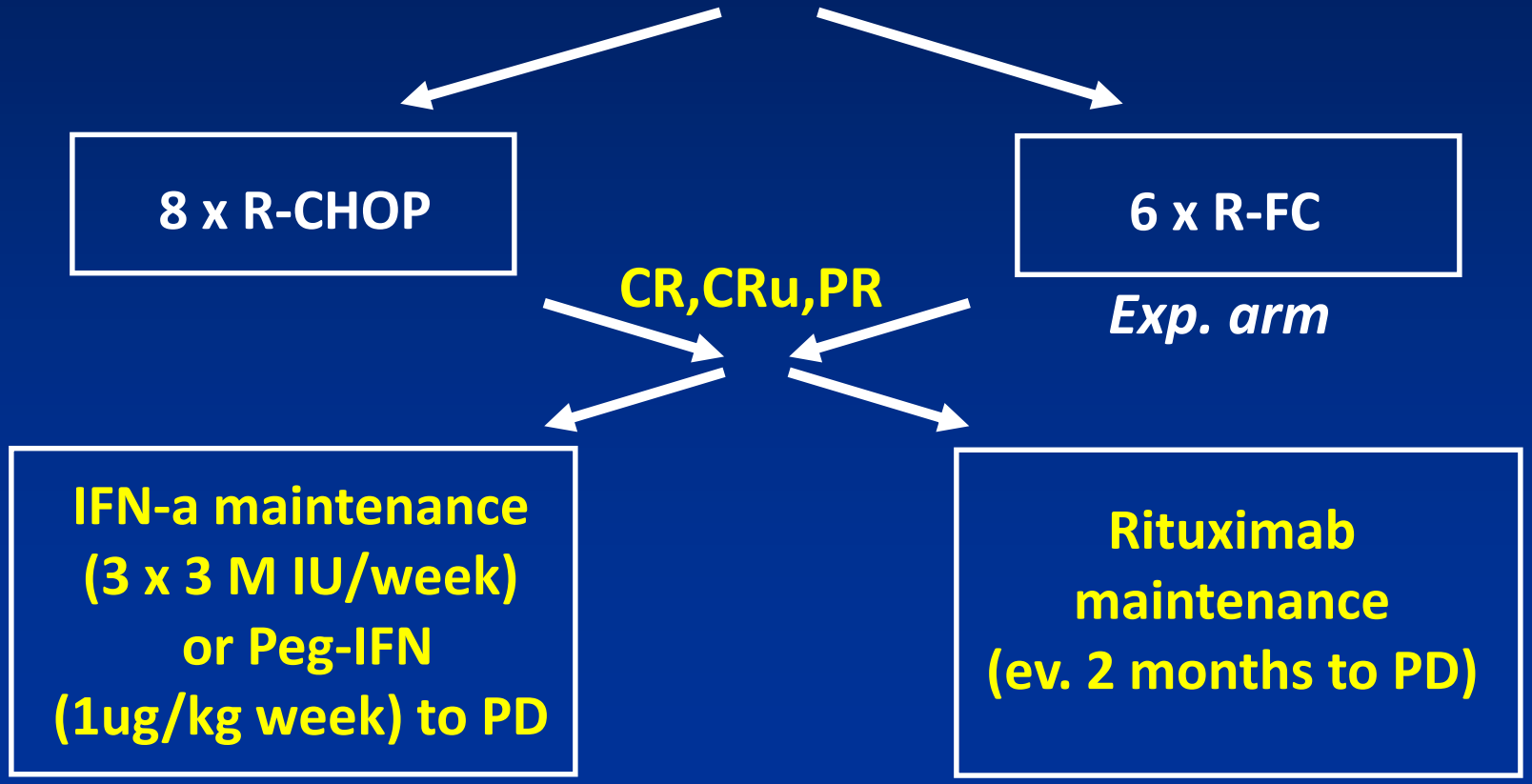
1st: is Flu-regimen better than CHOP?

2nd: does maintenance with Rituximab prolong remission?

First RCT for MCL Elderly

8 countries, n = 560 (Jan 2004-Oct 2010)

Newly diagnosed, >60 yr or frail; performance 0-2,
Stages II-IV, central PA review



JC Kluin-Neelemans et al N Engl J Med 2012;367:520-31

MCL Elderly: Overall survival
Induction R-CHOP *vs* R-FC
intention-to-treat analysis

More toxicity in FCR arm
Leading to less treatment* and more progression

And More R-FC patients than R-CHOP patients died in CR due to infection

Cause of death	R-FC	R-CHOP
Died in CR/PR	10%	4%
Infections	7%	4%
Second cancer	3%	1%

*23% of FC responders and 12% of CHOP responders did not complete therapy

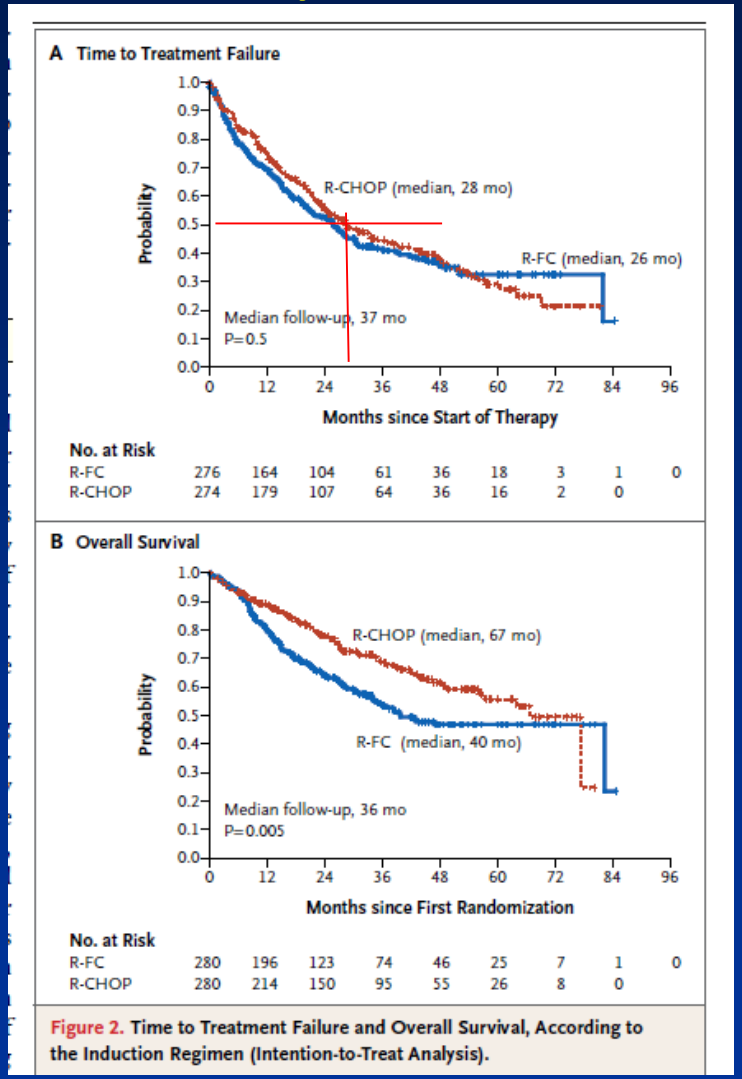
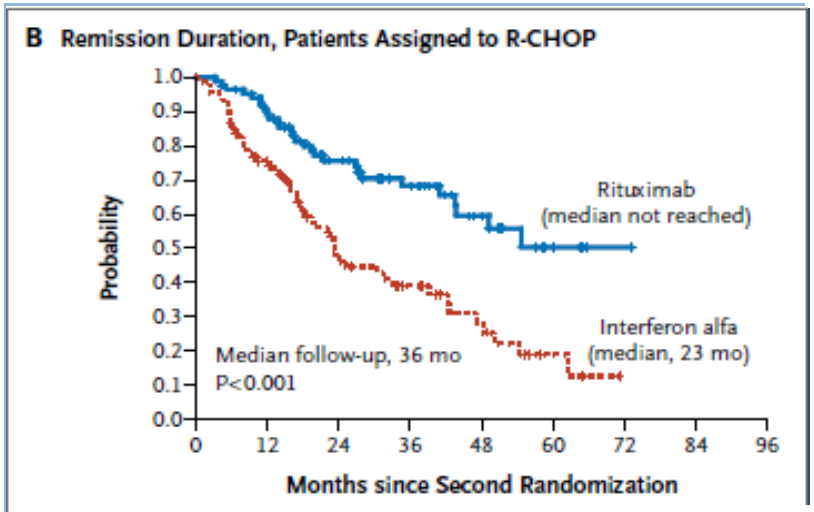
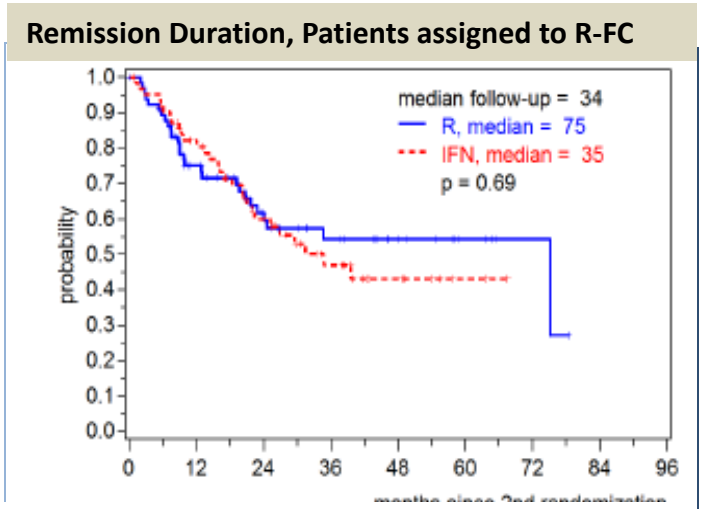


Figure 2. Time to Treatment Failure and Overall Survival, According to the Induction Regimen (Intention-to-Treat Analysis).

JC Kluin-Neelemans et al N Engl J Med 2012;367:520-31

Maintenance therapy: Rituximab vs Interferon α





Survival gain at 4 years among the patients who received R-CHOP (87% in the rituximab group vs. 63% in IFN; P = 0.005) but not among the patients who received R-FC (P = 0.48).

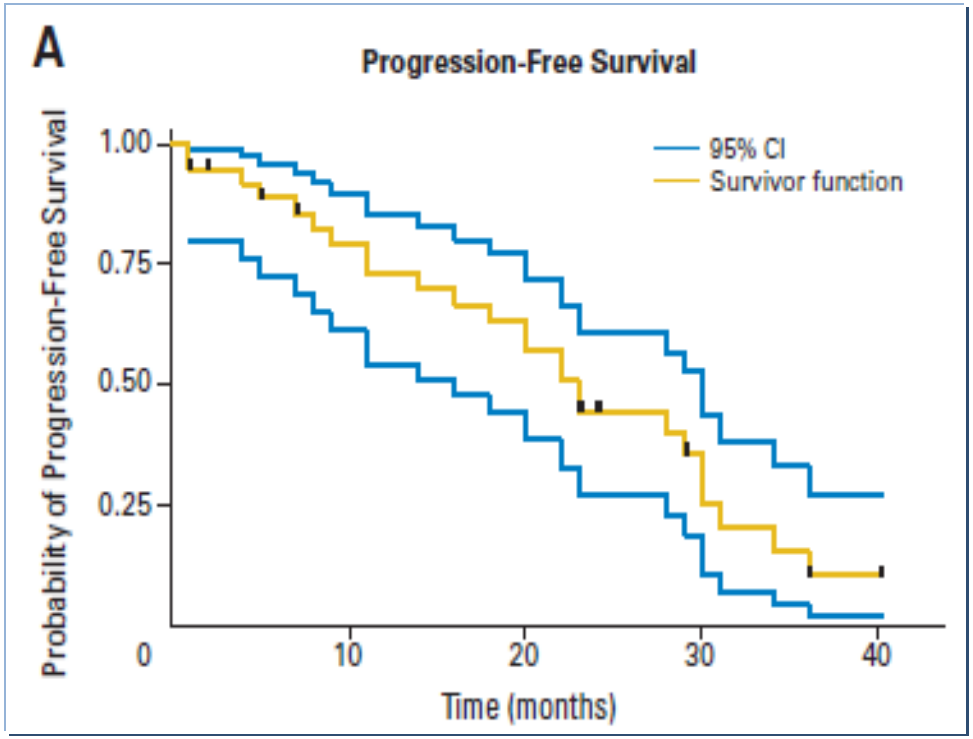
Toxic effects during the maintenance phase were more pronounced in the IFN group. After 1 year, maintenance therapy with IFN had been stopped in 49% of patients while they were in remission, whereas after 4 years, a premature stop of maintenance therapy with rituximab had occurred in only 28% of patients.

Kluin-Nelemans HC et al. NEJM 2012;367:520-31

R-CHOP+Bortezomib

	ORR (%)	CR (%)
36 untreated MCL	91	72

- Median age 66 (45-80)
- Median PFS 23 months
- Peripheral neuropathy 64%



Ruan J et al, JCO 2011

Bortezomib-Based Therapy for Newly Diagnosed Mantle-Cell Lymphoma

Tadeusz Robak, M.D., Huiqiang Huang, M.D., Jie Jin, M.D., Jun Zhu, M.D., Ting Liu, M.D., Olga Samoilova, M.D., Halyna Pylypenko, M.D., Gregor Verhoef, M.D., Ph.D., Noppadol Siritanaratkul, M.D., Evgenii Osmanov, M.D., Ph.D., Julia Alexeeva, M.D., Ph.D., Juliana Pereira, Ph.D., Johannes Drach, M.D., Jiri Mayer, M.D., Xiaonan Hong, M.D., Rumiko Okamoto, M.D., Lixia Pei, Ph.D., Brendan Rooney, Ph.D., Helgi van de Velde, M.D., Ph.D., and Franco Cavalli, M.D., for the LYM-3002 Investigators*

ABSTRACT

BACKGROUND

The proteasome inhibitor bortezomib was initially approved for the treatment of relapsed mantle-cell lymphoma. We investigated whether substituting bortezomib for vincristine in frontline therapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) could improve outcomes in patients with newly diagnosed mantle-cell lymphoma.

METHODS

In this phase 3 trial, we randomly assigned 487 adults with newly diagnosed mantle-cell lymphoma who were ineligible or not considered for stem-cell transplantation to receive six to eight 21-day cycles of R-CHOP intravenously on day 1 (with prednisone administered orally on days 1 to 5) or VR-CAP (R-CHOP regimen, but replacing vincristine with bortezomib at a dose of 1.3 mg per square meter of body-surface area on days 1, 4, 8, and 11). The primary end point was progression-free survival.

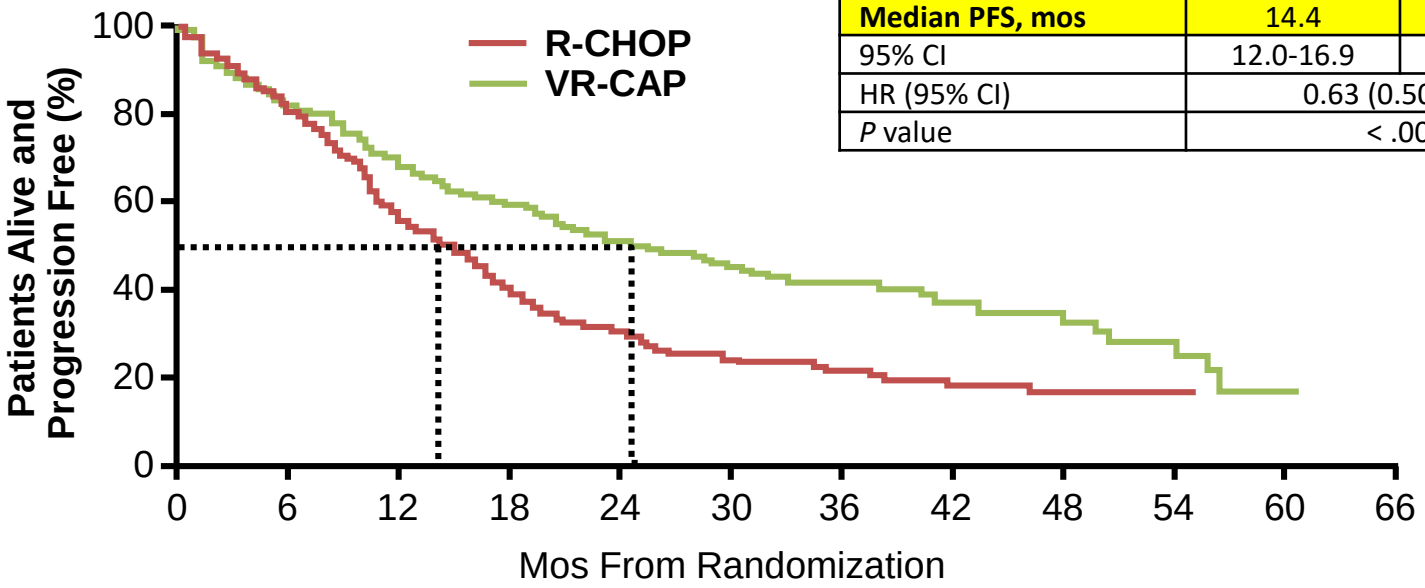
VR-CAP vs R-CHOP in transplantation-ineligible patients with newly diagnosed MCL

	VR-CAP group (n=140)	R-CHOP group (n=128)
Age, years		
Median (IQR)	65 (58–71)	66 (60–70)
≤65	75 (54%)	57 (45%)
>65	65 (46%)	71 (556%)

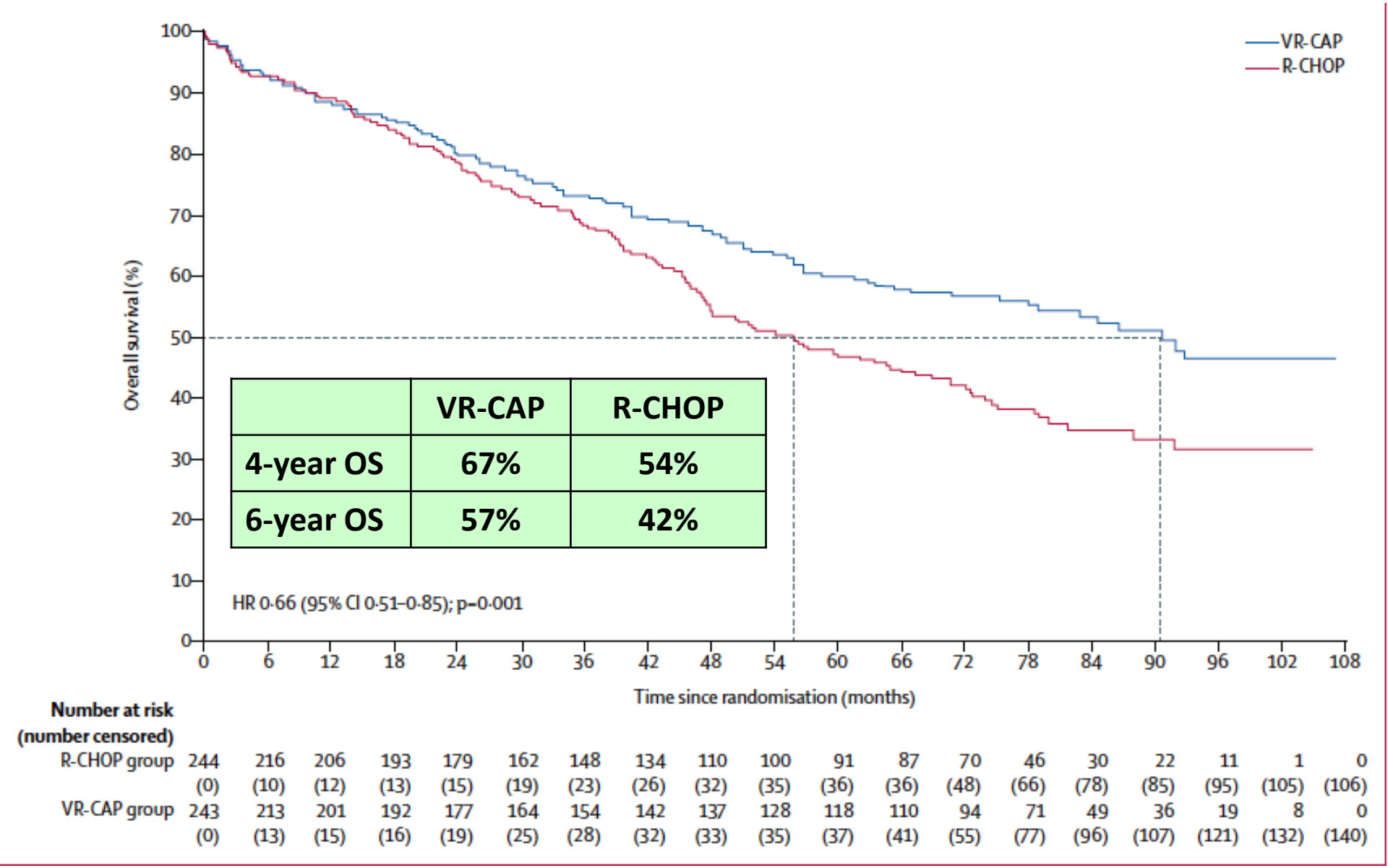
Robak et al. Lancet Oncol 2018

Superior PFS by IRC With VR-CAP vs R-CHOP: 59% Improvement

	R-CHOP	VR-CAP
Events, n	165	133
Median PFS, mos	14.4	24.7
95% CI	12.0-16.9	19.8-31.8
HR (95% CI)	0.63 (0.50-0.79)	
P value	< .001	



Additional Outcomes	R-CHOP	VR-CAP	OR	*P* Value
CR + CRu, %	**42**	53	1.69	.007
ORR (CR + CRu + PR), %	90	92	1.43	.275
Median duration of response, mos	15.1	36.5	NA	NA
4-yr OS rate, %	53.9	64.4	NA	NA

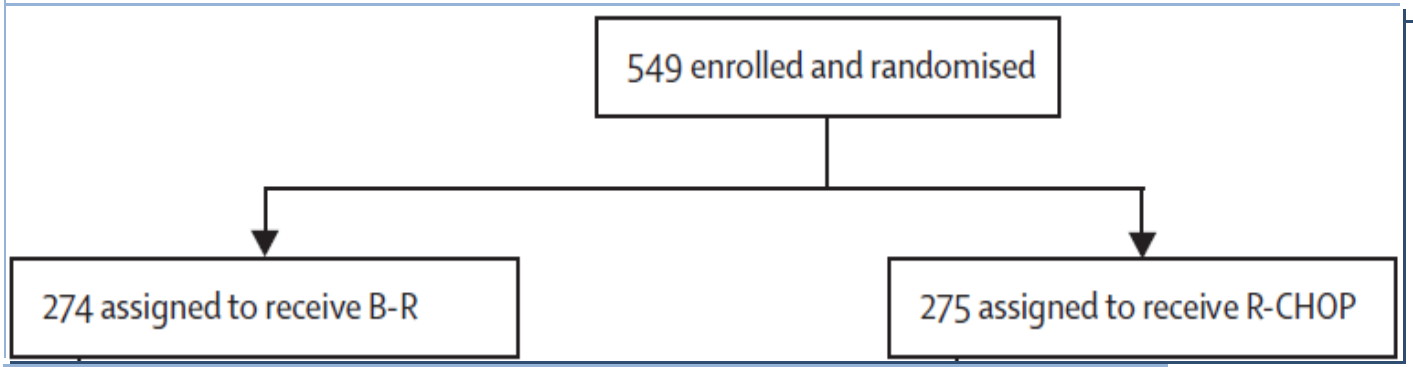


	VR-CAP	R-CHOP
4-year OS	67%	54%
6-year OS	57%	42%

Robak et al. Lancet Oncol 2018

Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial

Mathias J Rummel, Norbert Niederle, Georg Maschmeyer, G Andre Banat, Ulrich von Grünhagen, Christoph Losem, Dorothea Kofahl-Krause, Gerhard Heil, Manfred Welslau, Christina Balser, Ulrich Kaiser, Eckhart Weidmann, Heinz Dürk, Harald Ballo, Martina Stauch, Fritz Roller, Juergen Barth, Dieter Hoelzer, Axel Hinke, Wolfram Brugger, on behalf of the Study group indolent Lymphomas (StiL)



Histology		
Follicular	139 (53%)	140 (55%)
Mantle cell	46 (18%)	48 (19%)
Marginal zone	37 (14%)	30 (12%)
Lymphoplasmacytic*	22 (8%)	19 (8%)
Small lymphocytic	10 (4%)	11 (4%)
Low grade, unclassifiable	7 (3%)	5 (2%)

Median age 70 years (65-74)

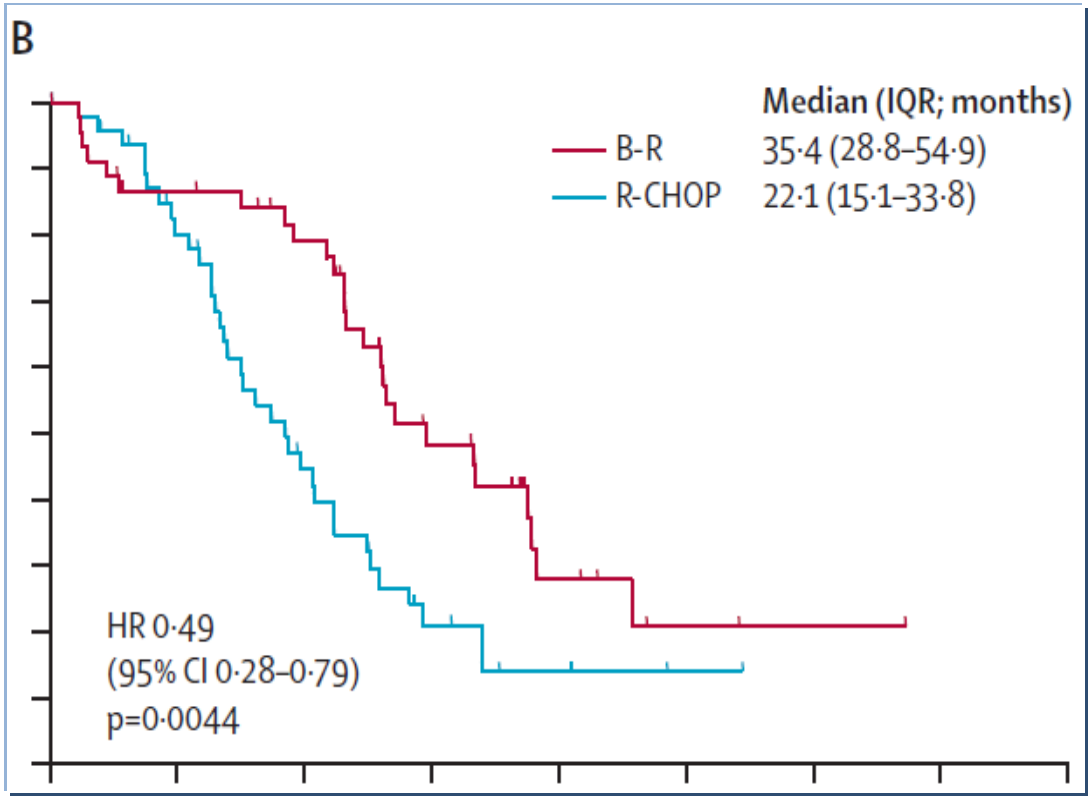
Rummel MJ et al. Lancet 2013;381:1203-10

Bendamustine plus Rituximab vs CHOP plus Rituximab

- **ORR did not differ** between the two treatment arms (242 [93%] of 261 patients in the BR group vs. 231 [91%] of 253 in the R-CHOP group)
- **CR rate was significantly increased in patients in the BR** group (104 [40%] vs. 76 [30%]; p.021).

	Grade 3–4	
	R-CHOP	B-R
Leucocytopenia	181 (72%)*	98 (37%)*
Neutropenia	173 (69%)*	77 (29%)*
Lymphocytopenia	106 (43%)	196 (74%)
Anaemia	12 (5%)	8 (3%)
Thrombocytopenia	16 (6%)	13 (5%)

	B-R (n=261)	R-CHOP (n=253)	p value
Alopecia	0	245 (100%)*	<0·0001
Paresthesia	18 (7%)	73 (29%)	<0·0001
Stomatitis	16 (6%)	47 (19%)	<0·0001
Skin (erythema)	42 (16%)	23 (9%)	0·024
Skin (allergic reaction)	40 (15%)	15 (6%)	0·0006
Infectious episodes	96 (37%)	127 (50%)	0·0025
Sepsis	1 (<1%)	8 (3%)	0·019



Rummel MJ et al. Lancet 2013;381:1203-10

Randomized trial of bendamustine-rituximab or R-CHOP/R-CVP in first-line treatment of indolent NHL or MCL: the BRIGHT study

Ian W. Flinn,[1] Richard van der Jagt,[2] Brad S. Kahl,[3] Peter Wood,[4] Tim E. Hawkins,[5] David MacDonald,[6] Mark Hertzberg,[7] Yiu-Lam Kwan,[8] David Simpson,[9] Michael Craig,[10] Kathryn Kolibaba,[11,12] Samar Issa,[13] Regina Clementi,[14] Doreen M. Hallman,[14] Mihaela Munteanu,[14] Ling Chen,[14] and John M. Burke[11,15]

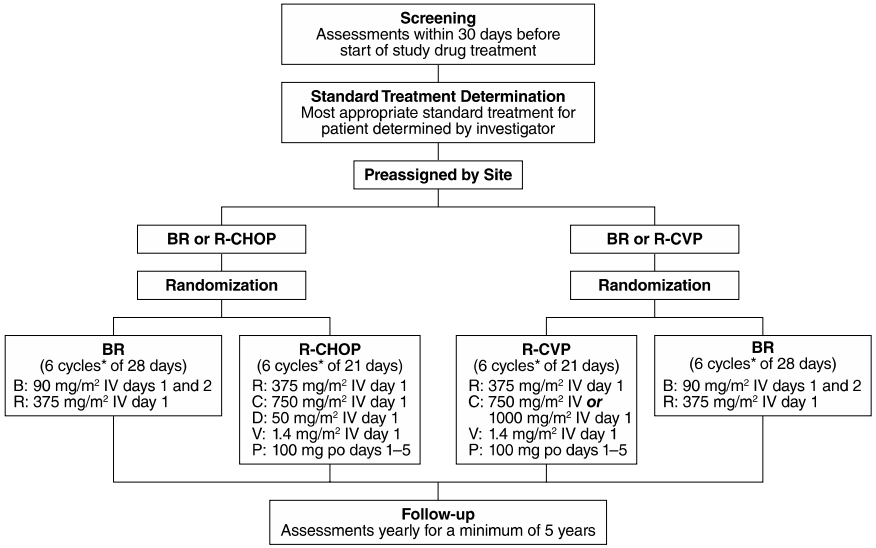


Table 1. Patient characteristics at baseline

Characteristic	BR (n = 224)	R-CHOP/R-CVP (n = 223)
Age, median, years (range)	60 (28–84)	58 (25–86)
Sex (male/female, %)	61/39	59/41
Baseline ECOG performance status, n (%)		
0	144 (64)	143 (64)
1	70 (31)	69 (31)
≥2	10 (4)	10 (4)
Histologic classification, n (%)		
Lymphoplasmacytic	5 (2)	6 (3)
Marginal zone	28 (12)	18 (8)
Mantle cell	36 (16)	38 (17)
Follicular, grade 1	84 (38)	70 (31)
Follicular, grade 2	70 (31)	90 (40)

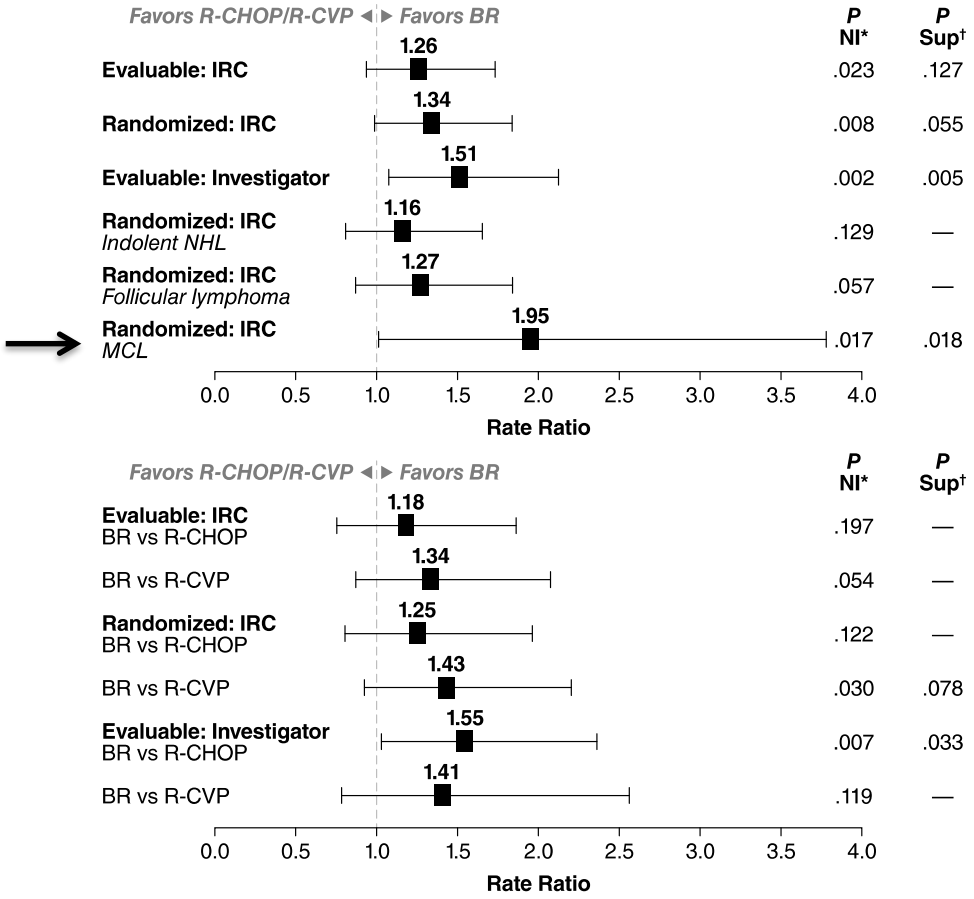
- 74 were MCL (ages: 64.5–74, median: 70)
- CR > in BR arm

Therapy	Patients
• BR:	223
• R-CHOP:	104
• R-CVP:	119

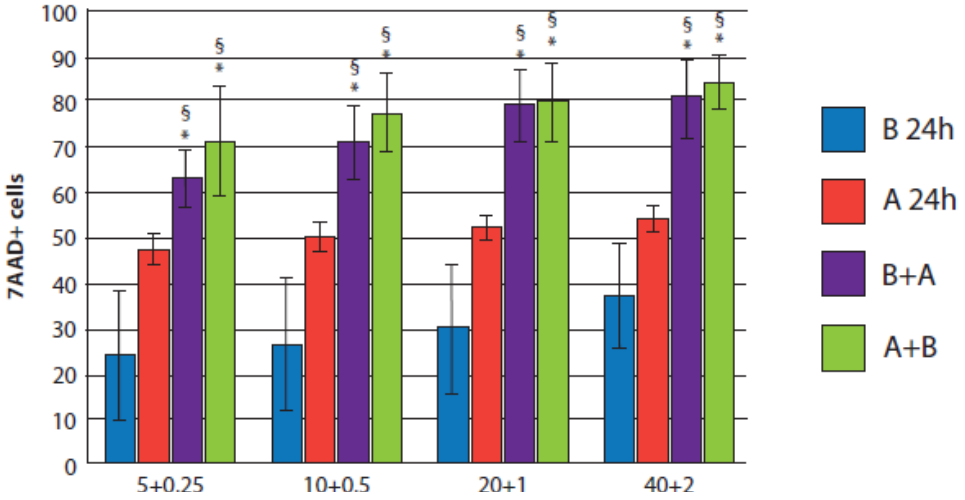
Table 3. IRC assessment of response by histologic subtypes (evaluable analysis)

Histologic subtype, n/N (%)	CR		CR + partial response	
	BR	R-CHOP/R-CVP	BR	R-CHOP/R-CVP
Indolent NHL	49/178 (28)	43/174 (25)	173/178 (97)	160/174 (92)
Follicular	45/148 (30)	37/149 (25)	147/148 (>99)	140/149 (94)
Marginal zone	5/25 (20)	4/17 (24)	23/25 (92)	12/17 (71)
Lymphoplasmacytic	0/5	1/6 (17)	3/5 (60)	6/6 (100)
MCL	17/34 (50)	P= 0.018 9/33 (27)*	32/34 (94)	28/33 (85)*

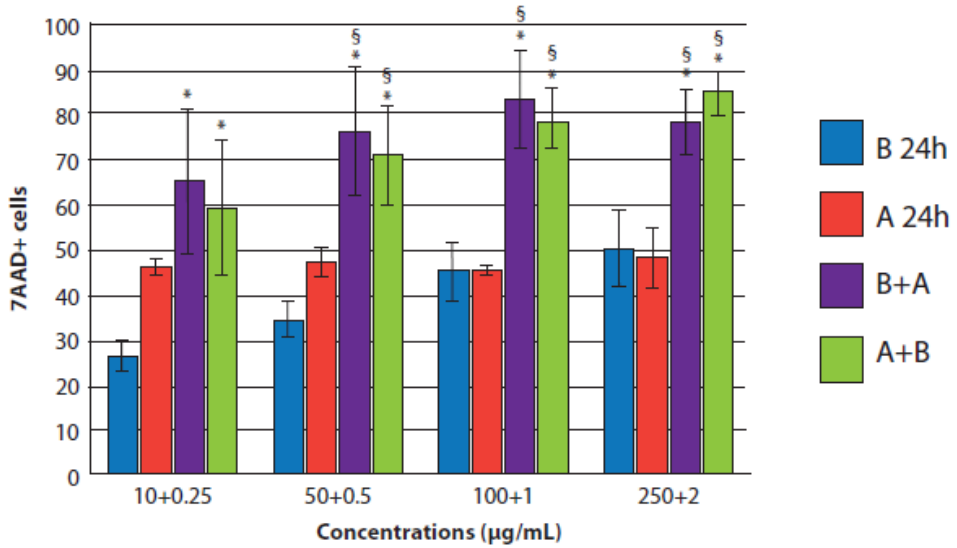
*R-CHOP, n = 22.



Classic MCL



Blastoid variant



Bendamustine (B) and Ara-C (A) are strongly synergistic in-vitro when cultured consecutively on MCL cell lines (CI<0.01)

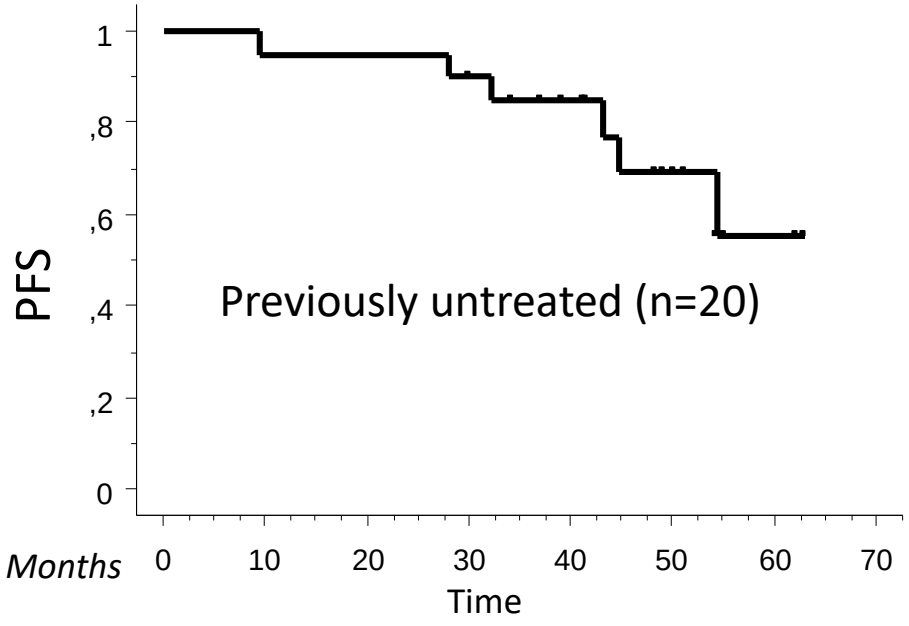
Visco et al, BCMD 2011

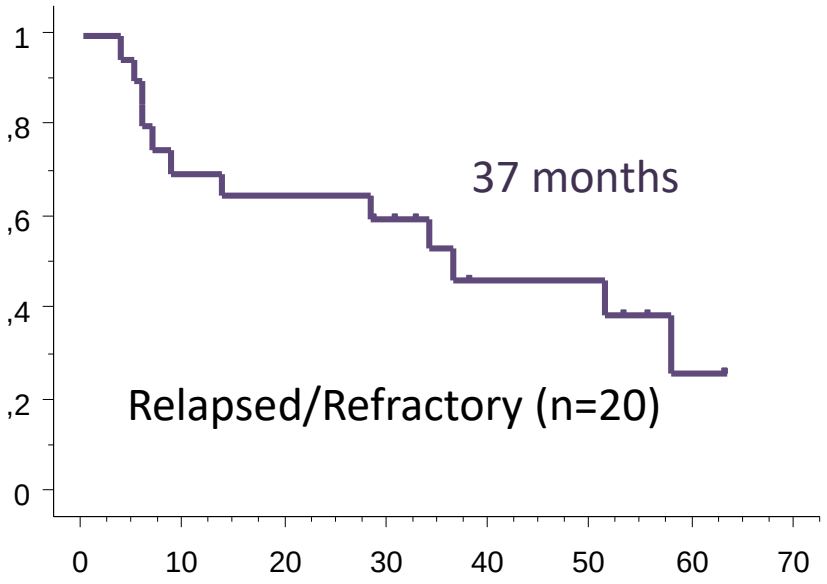
Rituximab, Bendamustine, Cytarabine (R-BAC)

Treatment	Day 1	Day 2	Day 3	Day 4
Rituximab 375 mg/m²	↓			
Bendamustine 70 mg/m²		↓	↓	
Ara-C 800 mg/m²		↓	↓	↓

	ORR (%)	CR (%)
Untreated	100	95
R/R	80	70

Median age 71 (54-82)
Median F/U **48 months** (28-63)





Visco C et al, JCO 2013

R-BAC PROTOCOL VI-1903

Hematologic Toxicity according to patient status

Delivered cycles: 173

	Overall (173)		Untreated (96)		R/R (77)		
Grade 3-4 event	N cycles	%	N cycles	%	N cycles	%	
Leukopenia	83	48	31	32	52	68	P<0.0001
Neutropenia	54	31	16	17	38	49	P<0.0001
Febrile neutropenia	7	4	4	4	3	4	p=n.s.
Thrombocytopenia	132	76	67	70	65	84	p=0.03
Anemia	85	49	41	43	44	57	p=n.s.

Data refer to cycles with at least 1 day of grade 3-4 event

Rituximab, bendamustine, and low-dose cytarabine as induction therapy in elderly patients with mantle cell lymphoma: a multicentre, phase 2 trial from Fondazione Italiana Linfomi

- Two stages, phase 2 study
- Introduction of MRD and CGA assessment
- Ara-C dose reduction to 500 mg/m^2
- Previously untreated >65 years or 60-65 unfit

- 1st patient 2 May 2012, last 25 Feb 2014

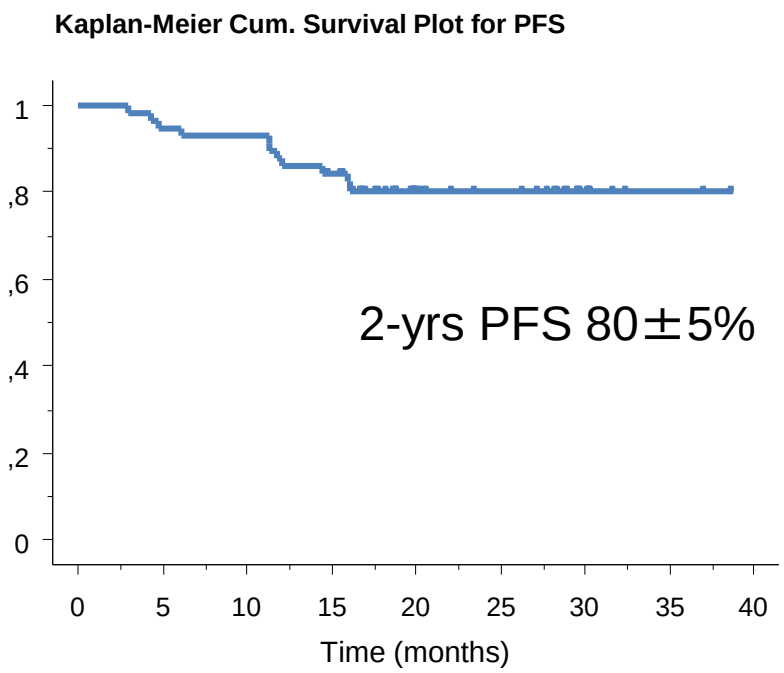
Visco et al . Lancet Oncol 2016

Patients Demographics and Disease Characteristics at Baseline

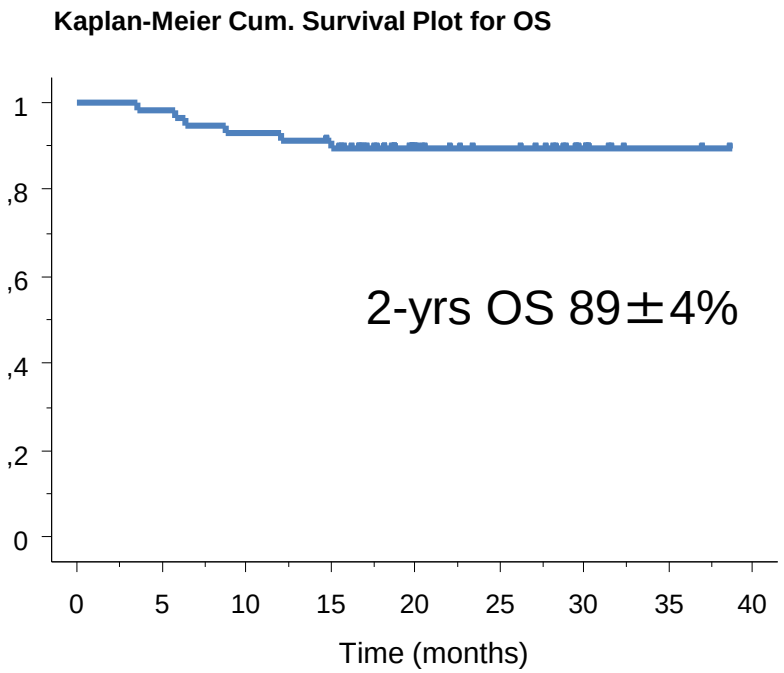
	Overall (57)	%
Age, years		
median	71	
range	61-79	
Gender		
male	43	75
female	14	25
Performance Status		
0-1	51	89
>1	6	11
Histology		
Classic MCL	52	91
Blastoid variant	5	9
AAS		
I-II	5	9
III-IV	52	91
MIPI risk category		
low risk	9	16
intermediate risk	29	51
high risk	19	33
BM involvement	36	63
Elevated LDH	20	35

Survival curves

PFS



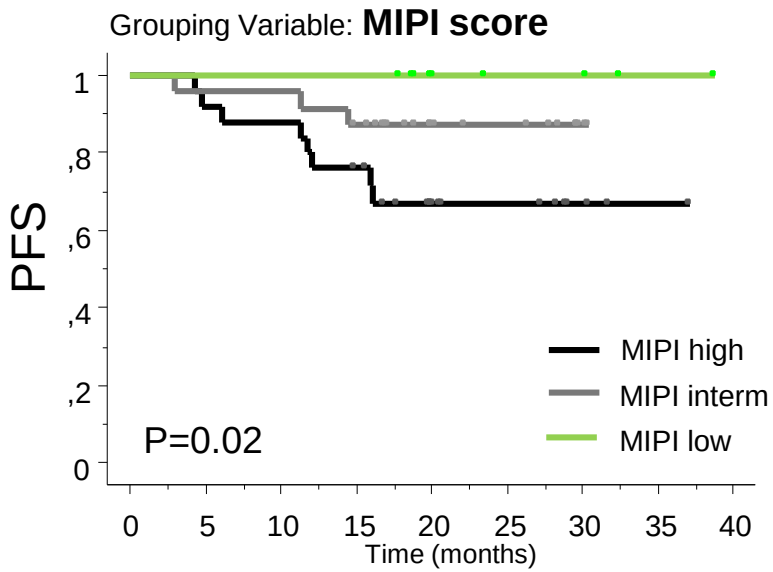
OS

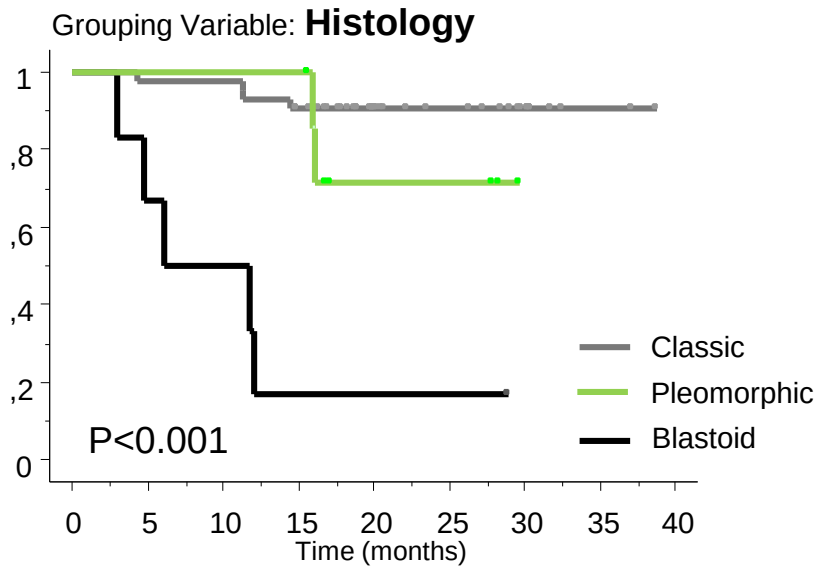


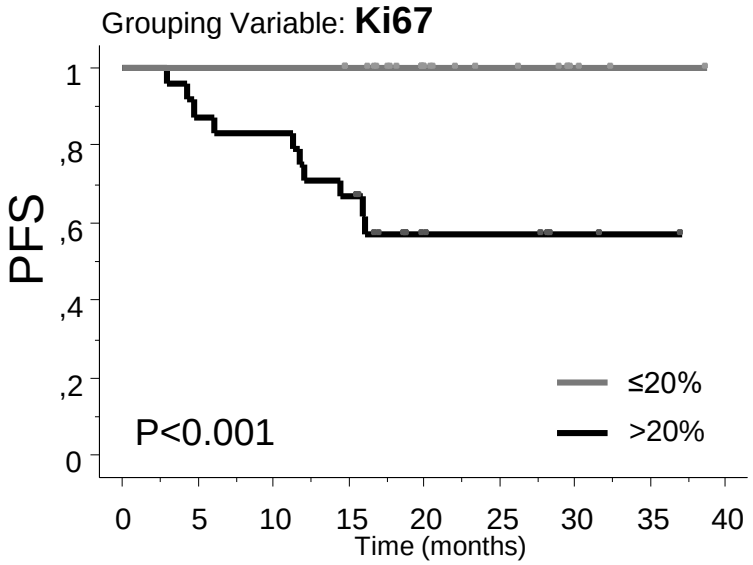
Median follow-up 22 months (15-38)

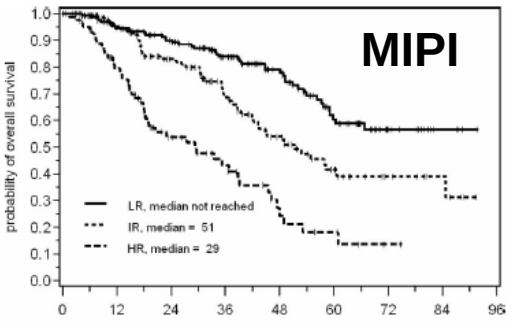
Visco et al . Lancet Oncol 2016

Survival curves

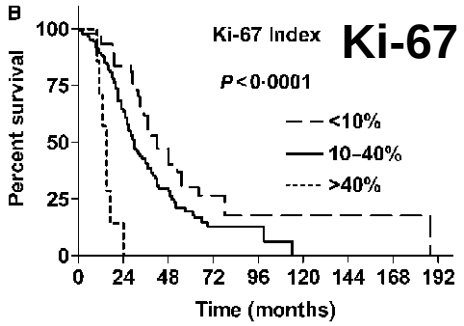








Hoster et al, Blood 2008

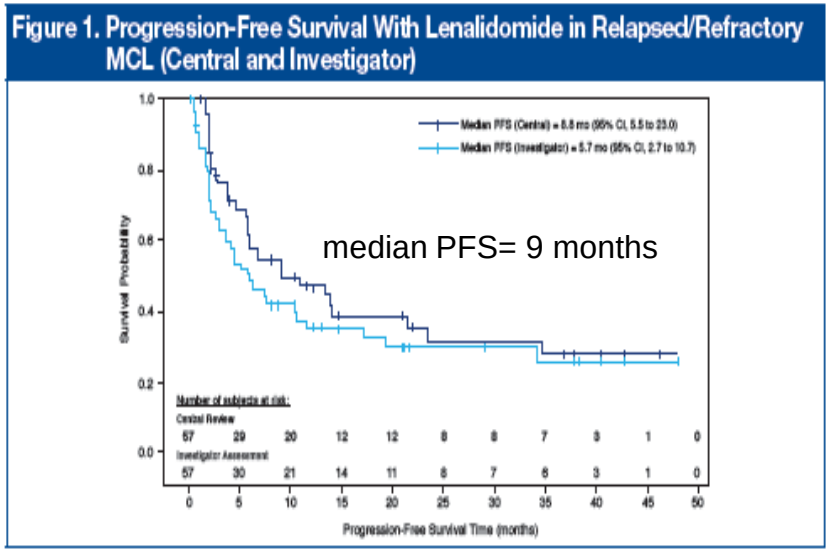


Tiemann et al BJH 2005

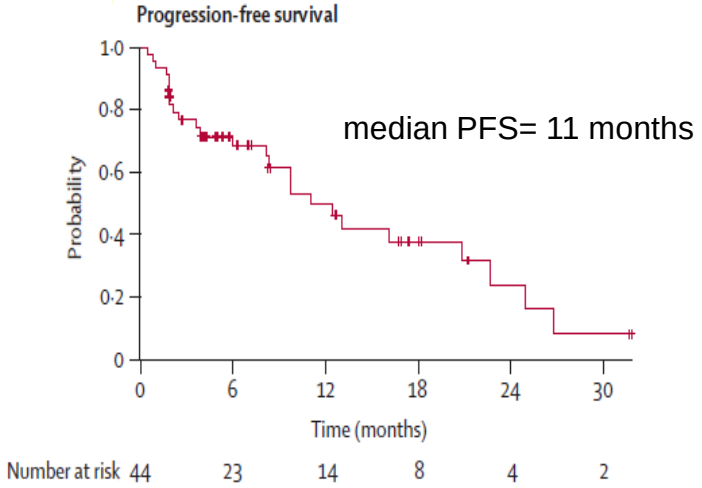
Visco et al . Lancet Oncol 2016

Lenalidomide monotherapy in MCL

Author	N.	ORR	CR/Cru	Median PFS (months)	Median DOR (months)
Wiernik 2008	15	53%	13%		
Haberman 2009	15	53%	20%	6	14
Eve 2012	26	31%	8%		
Wang 2012 (+ RTX)	**44**	**57%**	**36%**	**11**	**19**
Witzig 2011, Zinzani 2013	57	42%	12%	9	16
Goy ASH 2012 (Bortezomib R/R)	134	28%	8%	4	17
REVEAL 2013	66	39%	12%	12	



Zinzani et al 2013



Wang et al 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenalidomide plus Rituximab as Initial Treatment for Mantle-Cell Lymphoma

Jia Ruan, M.D., Ph.D., Peter Martin, M.D., Bijal Shah, M.D., Stephen J. Schuster, M.D., Sonali M. Smith, M.D., Richard R. Furman, M.D., Paul Christos, Dr.P.H., Amelyn Rodriguez, R.N., Jakub Svoboda, M.D., Jessica Lewis, P.A., Orel Katz, P.A., Morton Coleman, M.D., and John P. Leonard, M.D.

N ENGL J MED 373;19 NEJM.ORG NOVEMBER 5, 2015

Characteristic	Patients (N = 38)
Sex — no. (%)	
Male	27 (71)
Female	11 (29)
Age — yr	
Median	65
Range	42–86
ECOG performance status — no. (%)*	
0–1	37 (97)
>1	1 (3)
Ann Arbor stage III or IV — no. (%)	38 (100)
Lactate dehydrogenase level — no. (%)	
Normal	23 (61)
Elevated	15 (39)
Bone marrow involvement — no. (%)	
Yes	34 (89)
No	4 (11)
MIPI score — no. (%)†	
<5.7	13 (34)
5.7 to <6.2	13 (34)
≥6.2	12 (32)
IPI score — no. (%)‡	
0–1	6 (16)
2	18 (47)
3	10 (26)
4–5	4 (11)
Ki-67 index — no. (%)	
<30%	26 (68)
≥30%	8 (21)
Unavailable	4 (11)

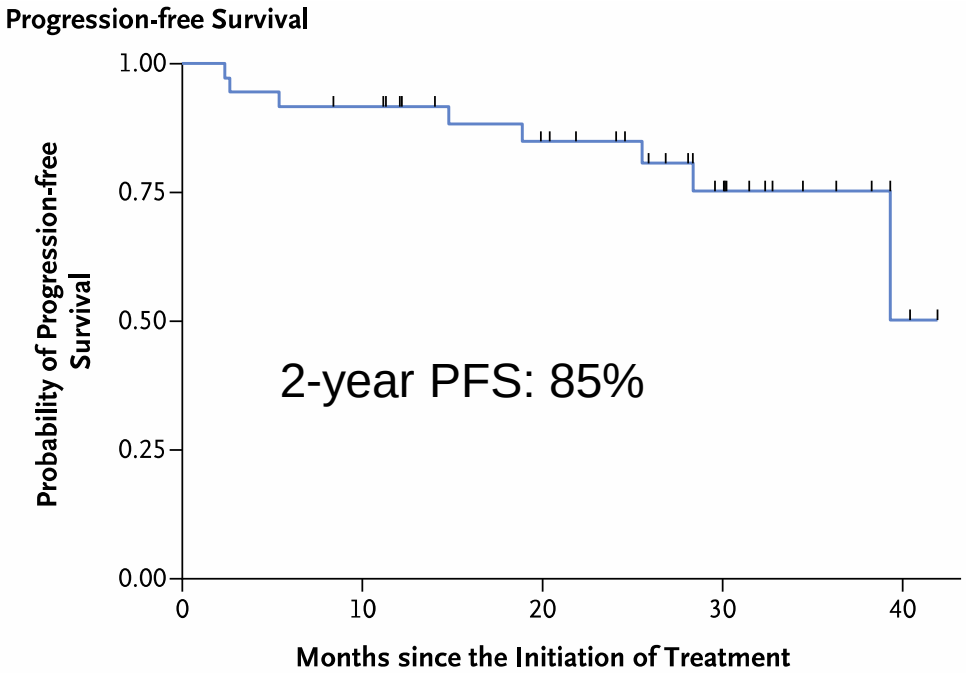
Table 2. Rates of Best Response at the Median Follow-up of 30 Months.

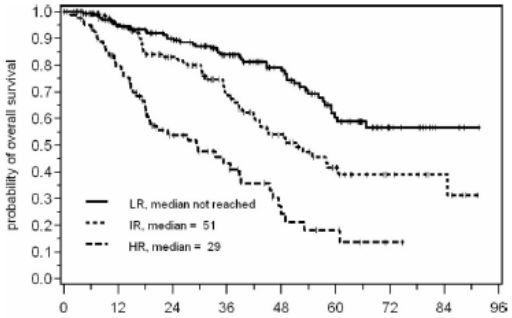
Response	Patients	Intention-to-Treat Population (N = 38)	Patients Who Could Be Evaluated (N = 36)
	no.	%	
Overall response	33	87	92
Complete response*	23	61	64
Partial response	10	26	28
Stable disease	1	3	3
Progressive disease†	2	5	6
Could not be evaluated‡	2	5	

Table 3. Survival and Follow-up Data.

Variable	Value
Median progression-free survival	Not reached
2-Yr progression-free survival — % of patients (95% CI)	85 (67–94)
2-Yr overall survival — % of patients (95% CI)	97 (79–99)
Follow-up time — mo	
Median	30
Range	10–42
Time to partial response — mo	
Median	3
Range	3–13
Time to complete response — mo*	
Median	11
Range	3–22

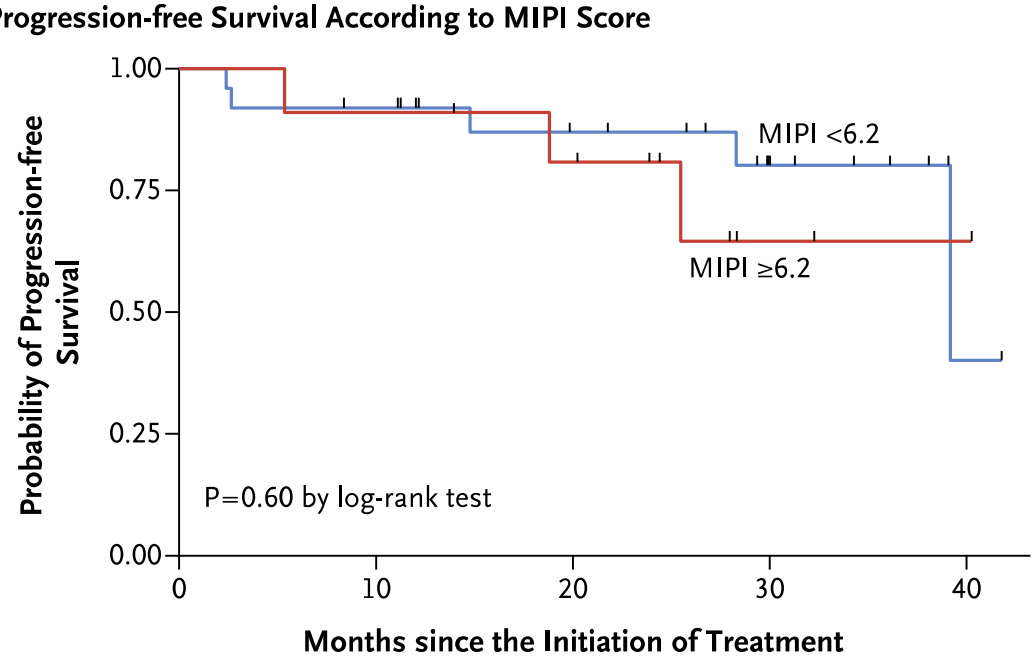
Ruan et al NEJM 2015



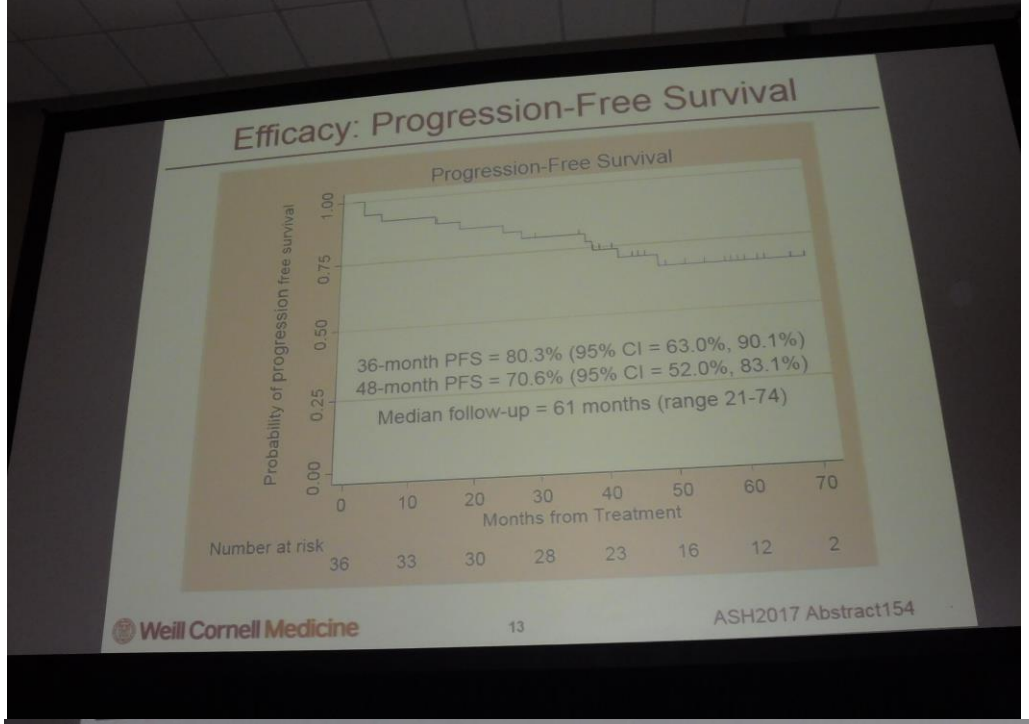


Hoster et al, Blood 2008

Neither the MIPI and IPI scores nor the Ki-67 index measurements were correlated with response to treatment or progression-free survival.



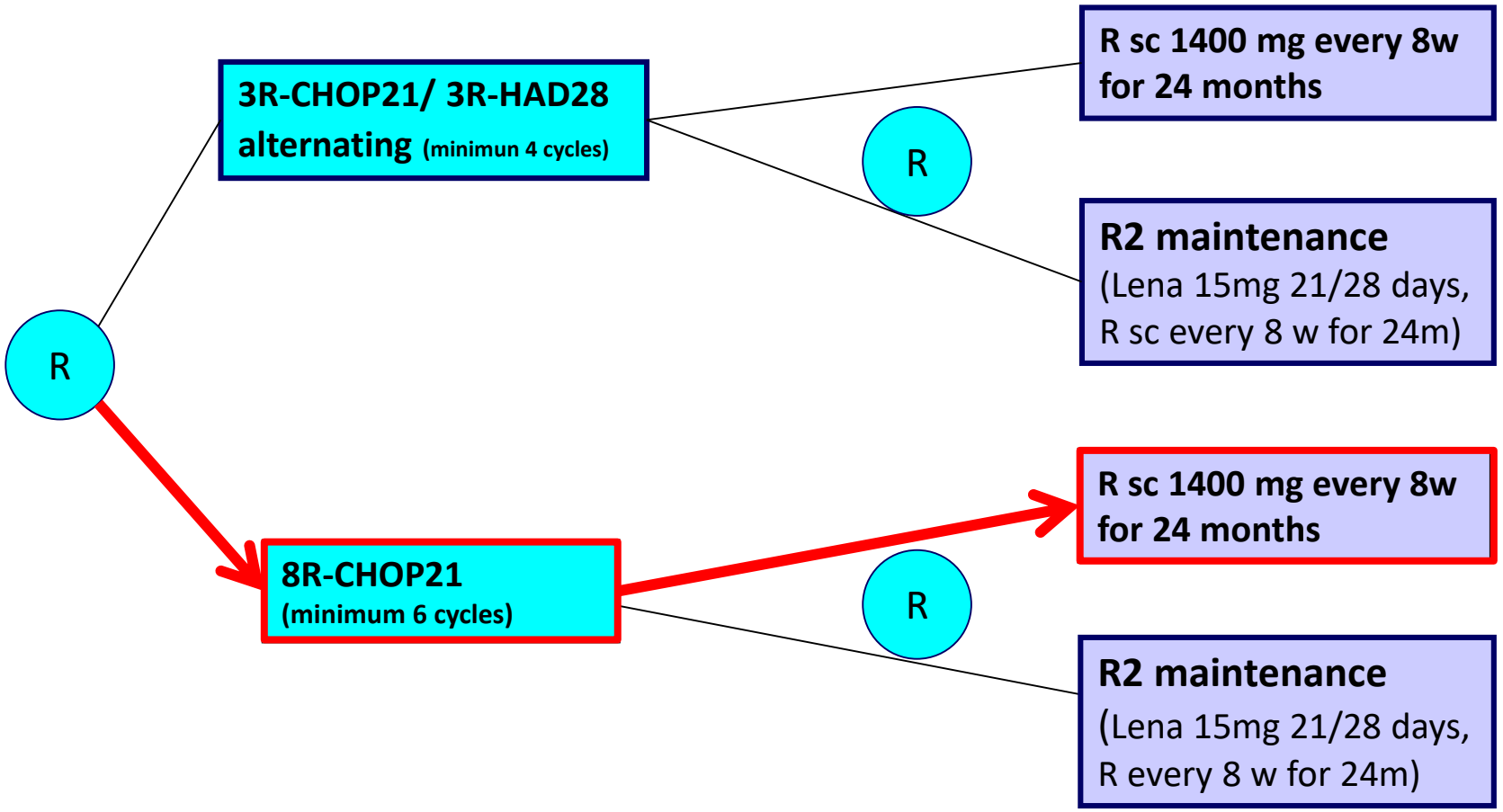
Ruan ASH 2017



Age, Gender	Study Phase	2nd Malignancy	Survival Status
74, Male	Induction	Squamous Cell CA	Alive, CR
	Maintenance	Squamous Cell CA	
60, Male	Maintenance	Squamous Cell CA	Alive, CR
	Maintenance	Basal Cell CA	
58, Male	Maintenance	Basal Cell CA	Alive, CR
86, Male	Maintenance	Melanoma in situ	Deceased
	Maintenance	Merkel Cell CA	
68, Male	Maintenance	Pancreatic CA	Deceased
66, Male	Induction	Melanoma in situ	Alive, PR

Events	Induction		Maintenance	
	Any	Grade≥3	Any	Grade≥3
Hematologic				
Neutropenia	68%	42%	66%	42%
Anemia	47%	8%	32%	3%
Thrombocytopenia	29%	11%	37%	5%
Febrile neutropenia	3%	3%	5%	5%
Infectious				
URI	24%	0	45%	0
UTI	11%	0	21%	5%
Sinusitis	5%	0	13%	0
Cellulitis	5%	0	11%	3%
Pneumonia	3%	3%	8%	8%

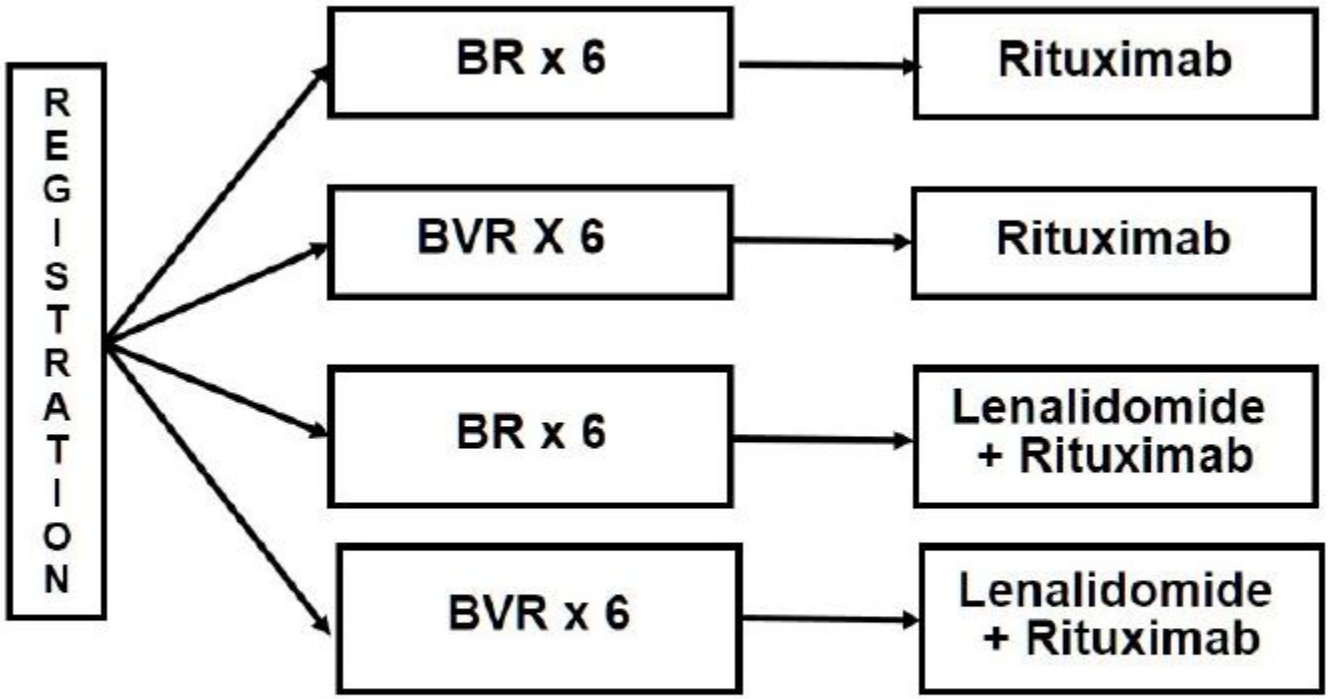
MCL R2 ELDERLY : STUDY DESIGN



NCT01865110

E1411 North American Intergroup Trial

Accrual to E1411 is ongoing and may define a new standard of care, particularly in older individuals with MCL.



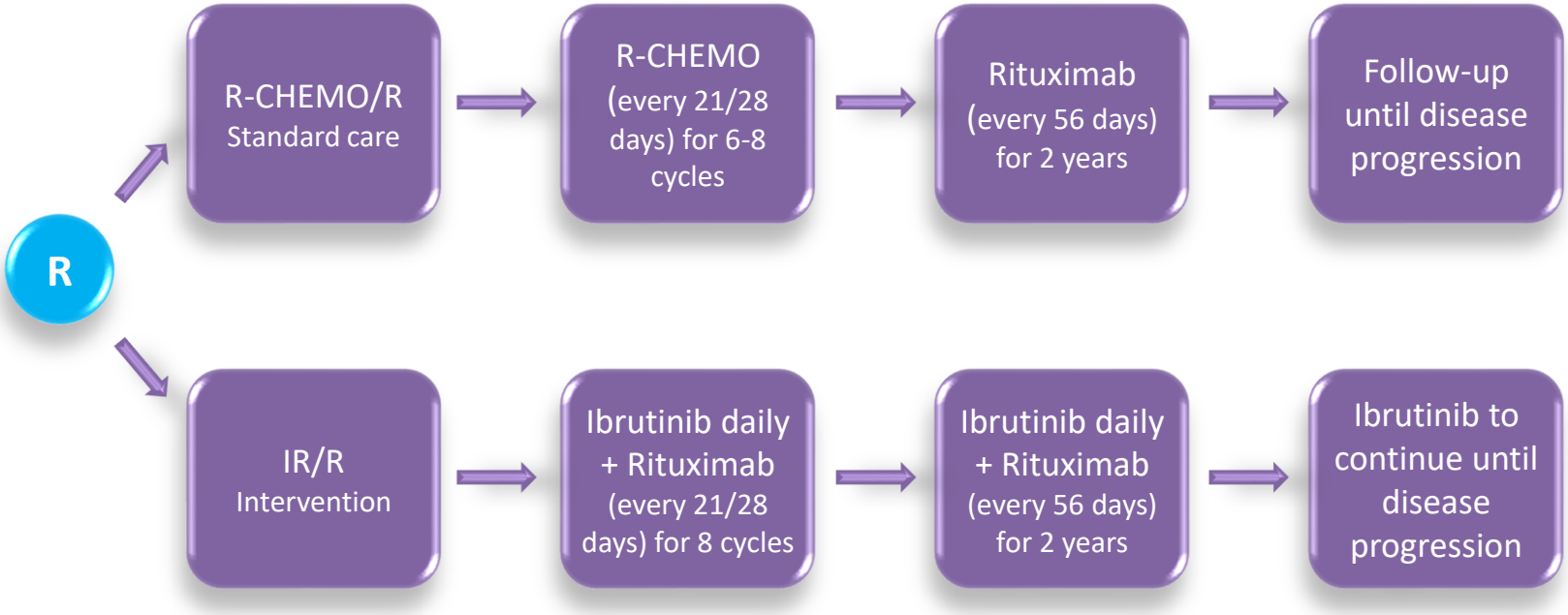
B=bendamustine, R=rituximab, V=bortezomib

Schema of E1411. Maintenance therapy is administered for 2 years.

NCT01415752

ENRICH – NCRI multicentre Randomised open label phase II/III trial of Rituximab & Ibrutinib *vs* Rituximab & CHemotherapy in Elderly mantle cell lymphoma

CANCER RESEARCH UK



Sinossi

Rituximab, bendamustina e citarabina seguiti da venetoclax (V-RBAC) in pazienti anziani, ad alto rischio con linfoma mantellare

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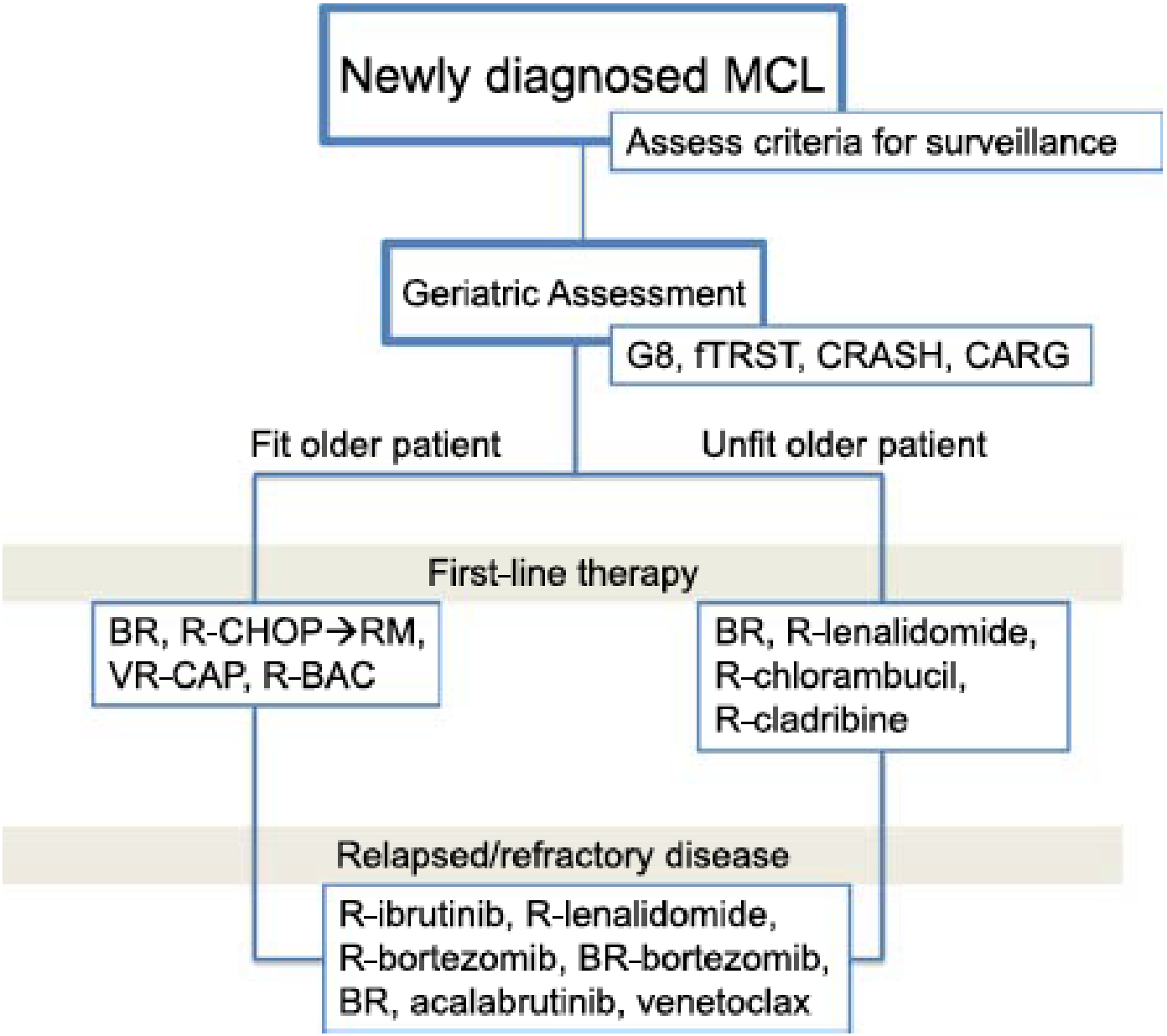
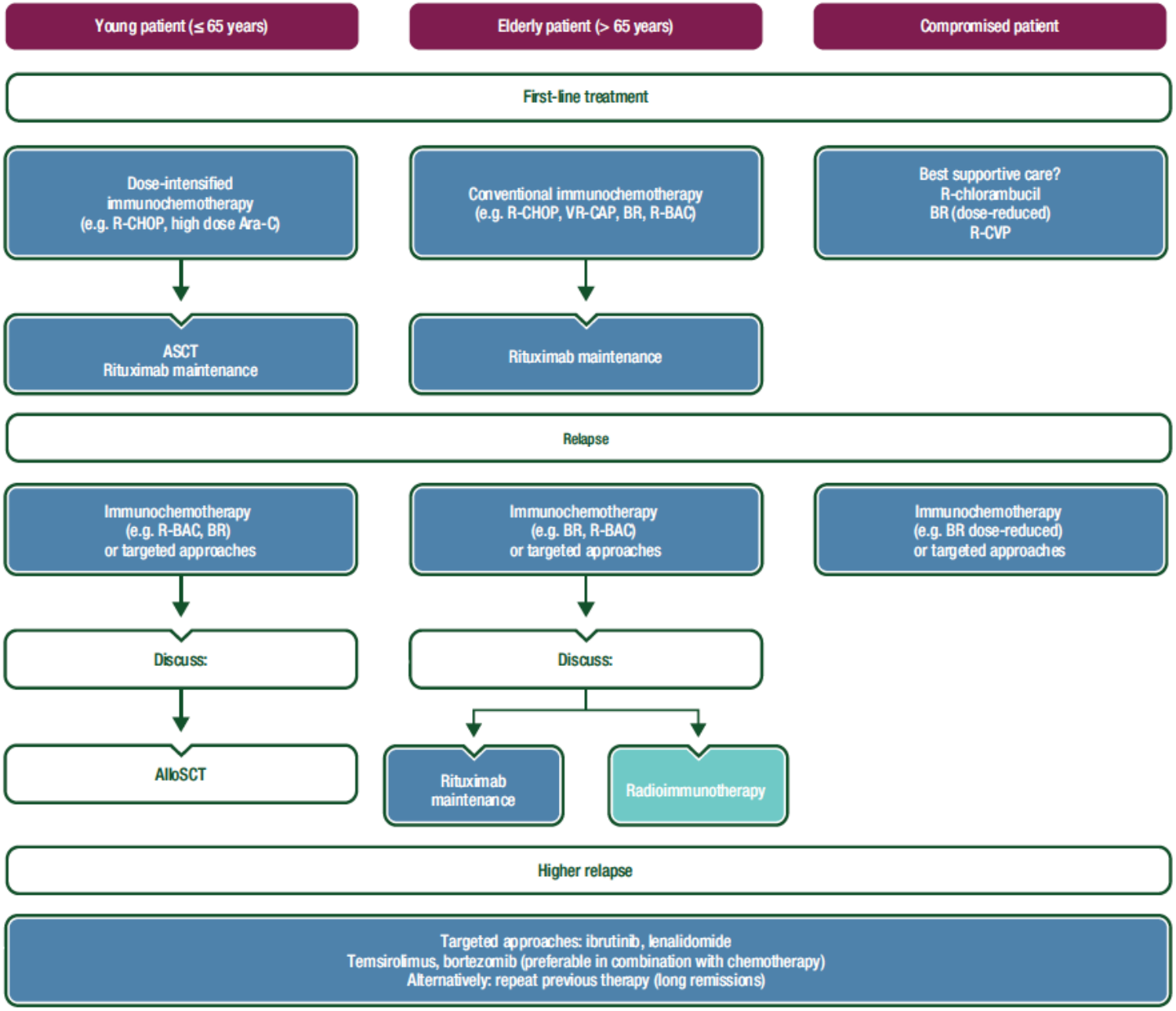
PROTOCOL

TITLE: Phase 3 Study of Ibrutinib in Combination with Venetoclax in Subjects with Mantle Cell Lymphoma

PROTOCOL NUMBER: PCYC-1143-CA


Newly diagnosed MCL
Assess criteria for surveillance
Geriatric Assessment
G8, fTRST, CRASH, CARG
Fit older patient
Unfit older patient
First-line therapy
BR, R-CHOP→RM, VR-CAP, R-BAC
BR, R-lenalidomide, R-chlorambucil, R-cladribine
Relapsed/refractory disease
R-ibrutinib, R-lenalidomide, R-bortezomib, BR-bortezomib, BR, acalabrutinib, venetoclax

Pease 2017



Dreyling ESMO Guidelins 2017

How I treat elderly patients with non indolent MCL

	"FIT"*	"UNFIT"	"FRAGILE"
1L	**Studio clinico** **R-BAC 500**	**Studio clinico** **RB**	**RB adattato**
Salvataggio	**Studio clinico** **RB** **(R)-Ibrutinib** **(R) Lenalidomide** **…**	**Studio clinico** **RB** **(R)-Ibrutinib** **(R) Lenalidomide** **…**	

*: età 65-70: considerare consolidamento con ASCT

Osservazione nelle forme indolenti