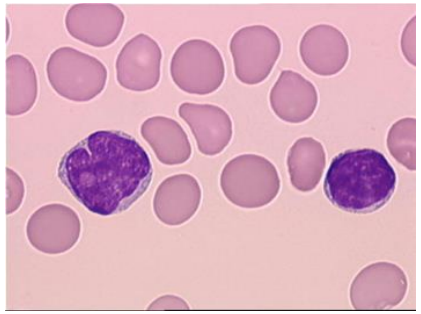
MANTLE CELL LYMPHOMA:

AUF DEM WEG ZUR HEILUNG ?



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Mantle cell lymphoma
Disclosures

https://bureaucracyincts.eu

Research Support (institution)	**Abbvie, Bayer, BMS/Celgene, Gilead/Kite, Janssen, Roche**
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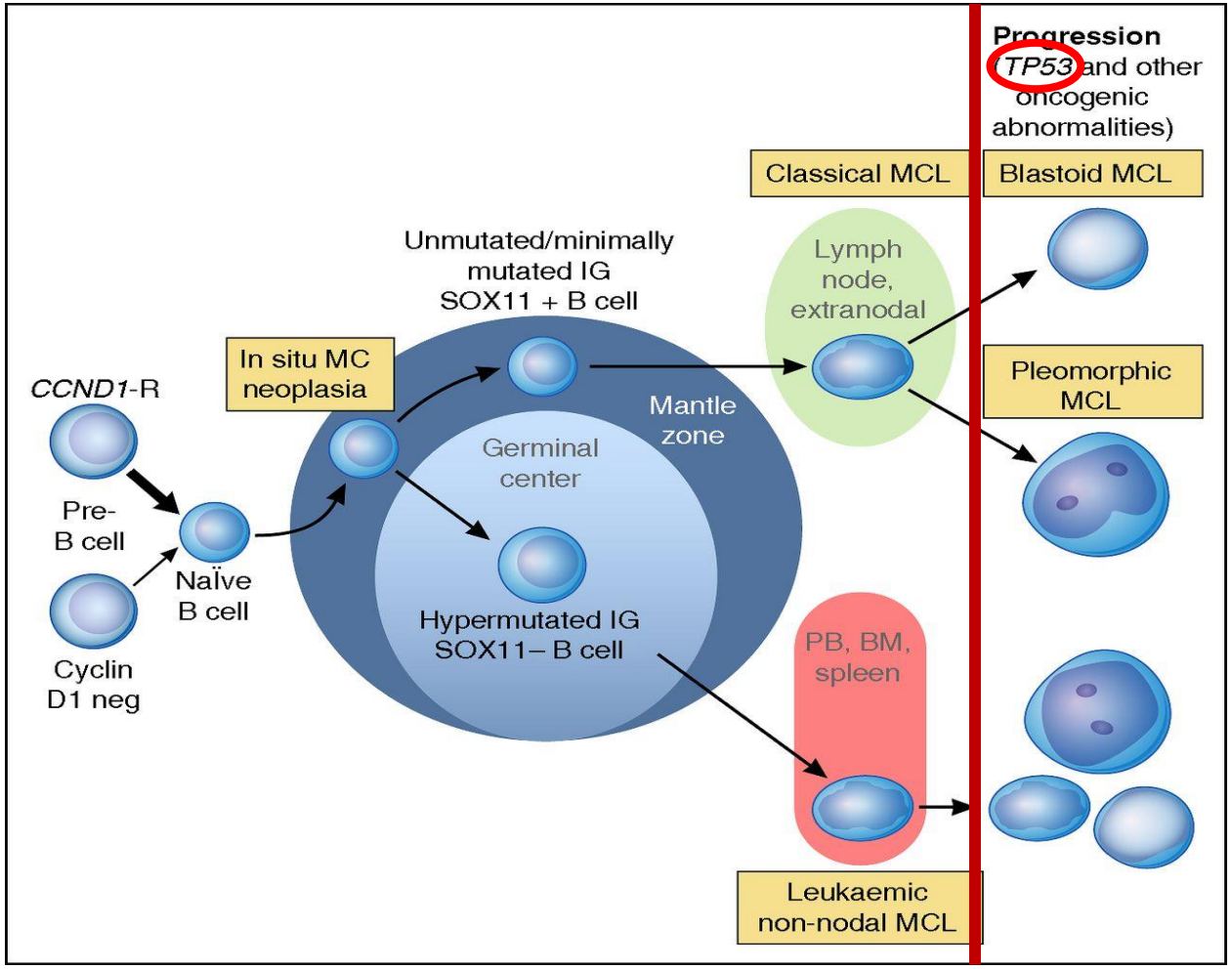
Mantle cell lymphoma
Overview

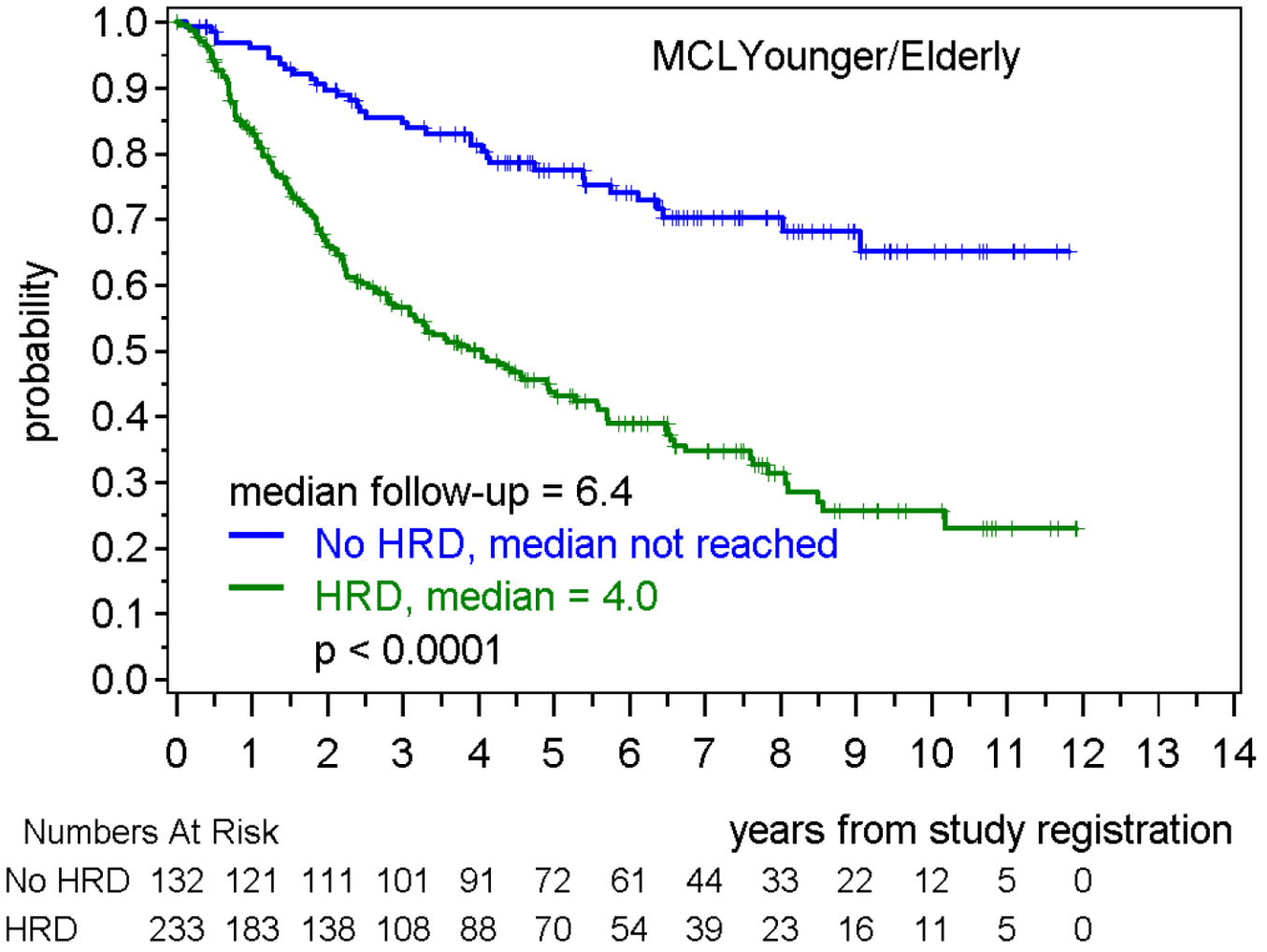
- molecular risk profile
- First line: chemotherapy standards
- targeted approaches

Mantle cell lymphoma
Spectrum of disease



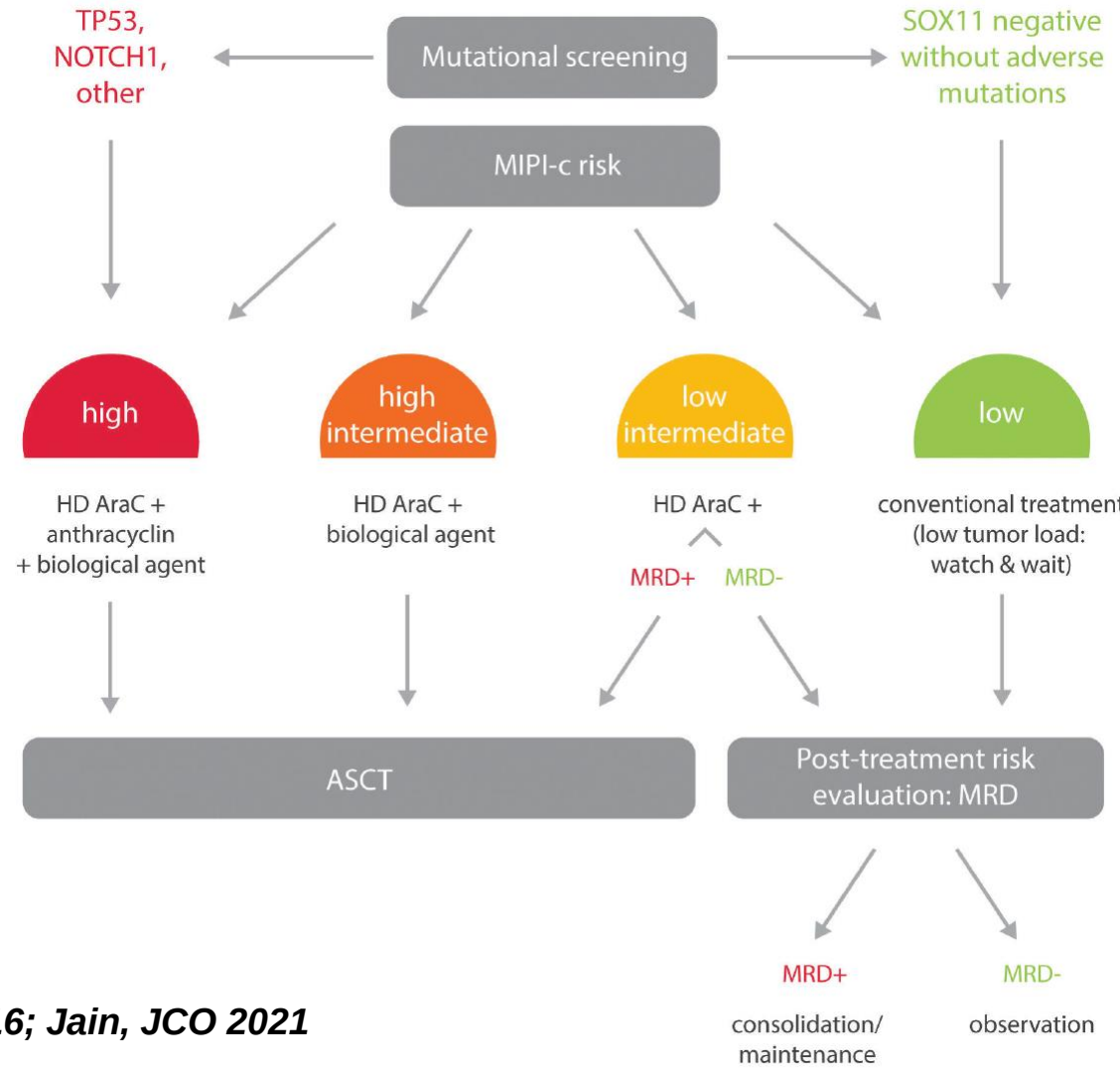
Dreyling, Ann Oncol 2017

High risk Mantle cell lymphoma
Overall survival (n=465)



Scheubeck, Leukemia 2023

European MCL Network
Suggested therapeutic algorithm

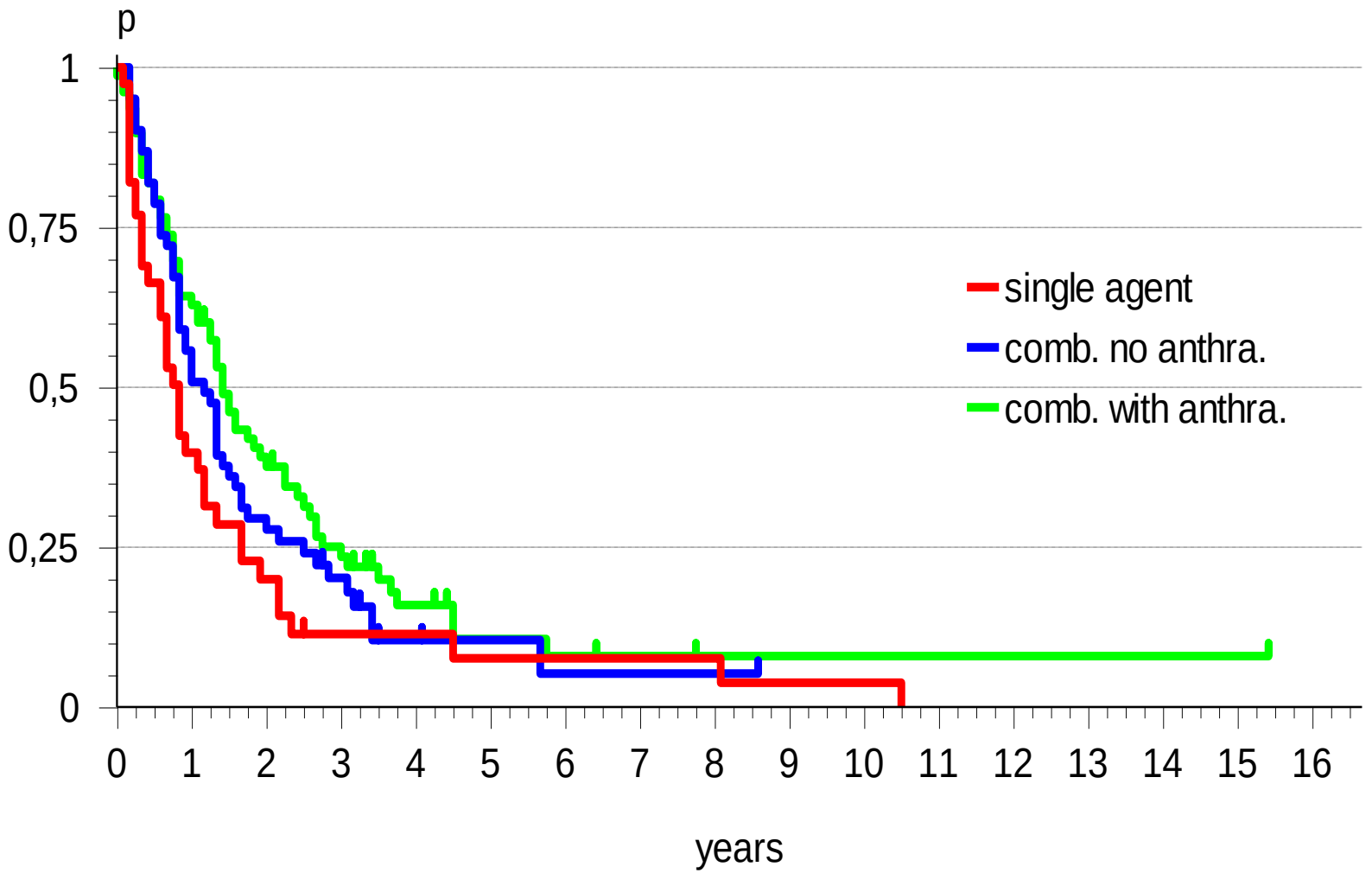


Dreyling, Haematologica 2016; Jain, JCO 2021

Multicenter Evaluation of MCL

Annexcy Criteria fulfilled

event free interval after chemotherapy in stages III + IV



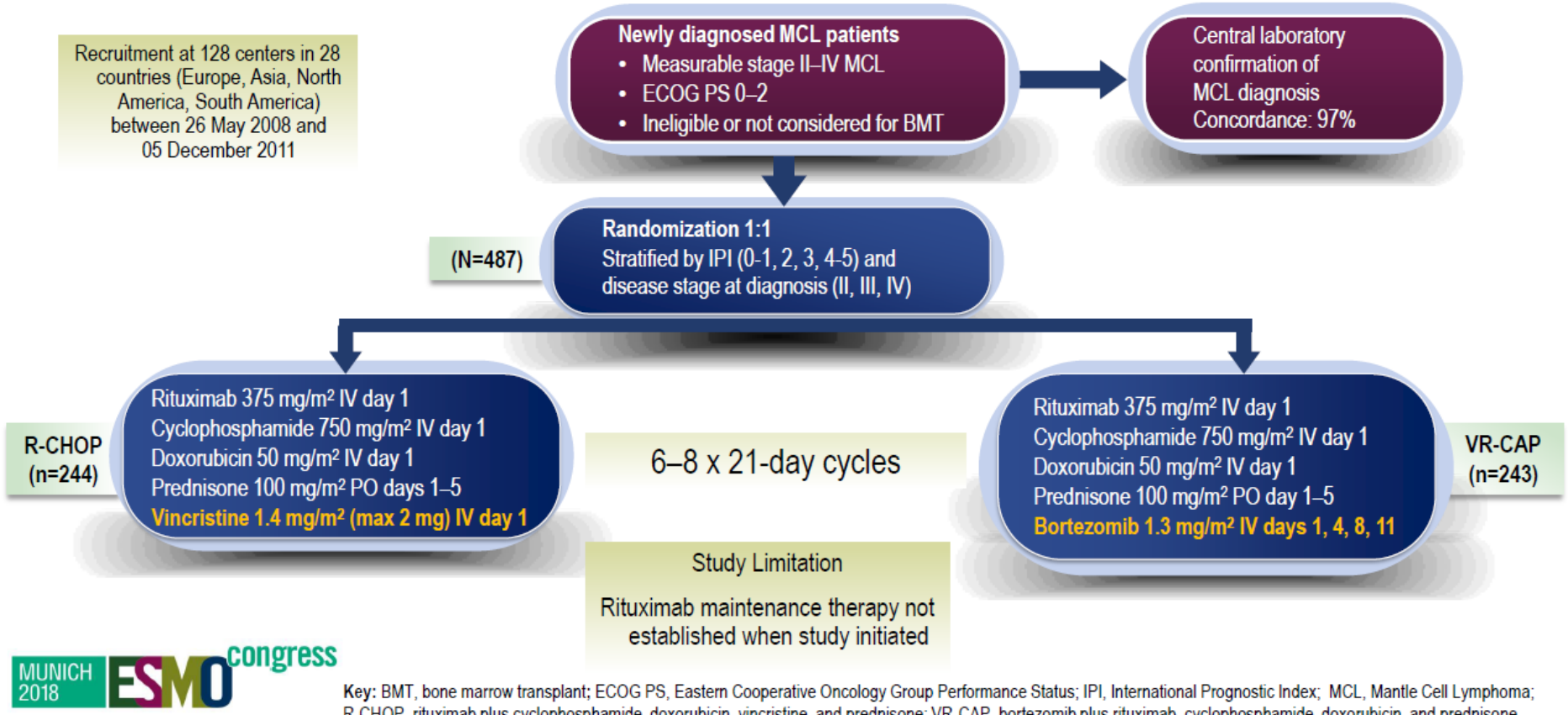
Dreyling, ASCO 1999

Therapeutic algorithm

young patient (≤65)	elderly patient (>65)	compromised patient
First line treatment		
dose-intensified immuno-chemotherapy (R-CHOP, high dose Ara-C) ⇒ Autologous SCT ⇒ Rituximab maintenance	conventional immuno-chemotherapy (VR-CAP, R-CHOP,BR, R-BAC) ⬇ Rituximab maintenance	Best supportive care? R-Chlorambucil BR (dose-reduced) R-CVP
1. relapse		
immuno-chemotherapy (R-BAC, BR) or targeted approaches ⬇ discuss: - allogeneic SCT	immuno-chemotherapy (BR, R-BAC) or targeted approaches ⬇ discuss: - Rituximab maintenance - radioimmunotherapy	Immuno-chemotherapy (BR) or targeted approaches
higher relapse		
Targeted approaches: Ibrutinib, Lenalidomide, Temsirolimus, Bortezomib (preferable in combination) Alternatively: repeat previous therapy (long remissions)		

Dreyling, ESMO CR MCL 2017 (updated)

VR-CAP vs. R-CHOP

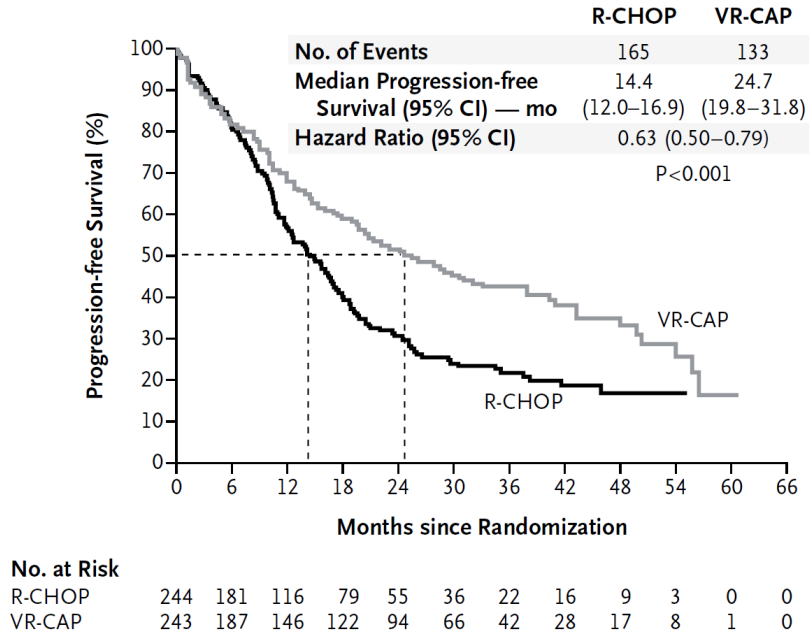


Key: BMT, bone marrow transplant; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IPI, International Prognostic Index; MCL, Mantle Cell Lymphoma; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone; VR-CAP, bortezomib plus rituximab, cyclophosphamide, doxorubicin, and prednisone

Cavalli, ESMO 2018

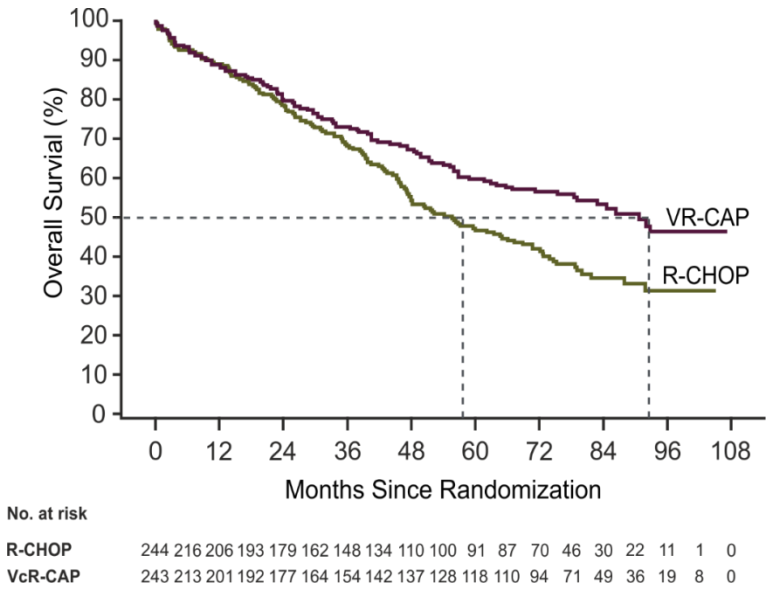
VR-CAP vs. R-CHOP

Progression-free Survival



Robak, NEJM 2015

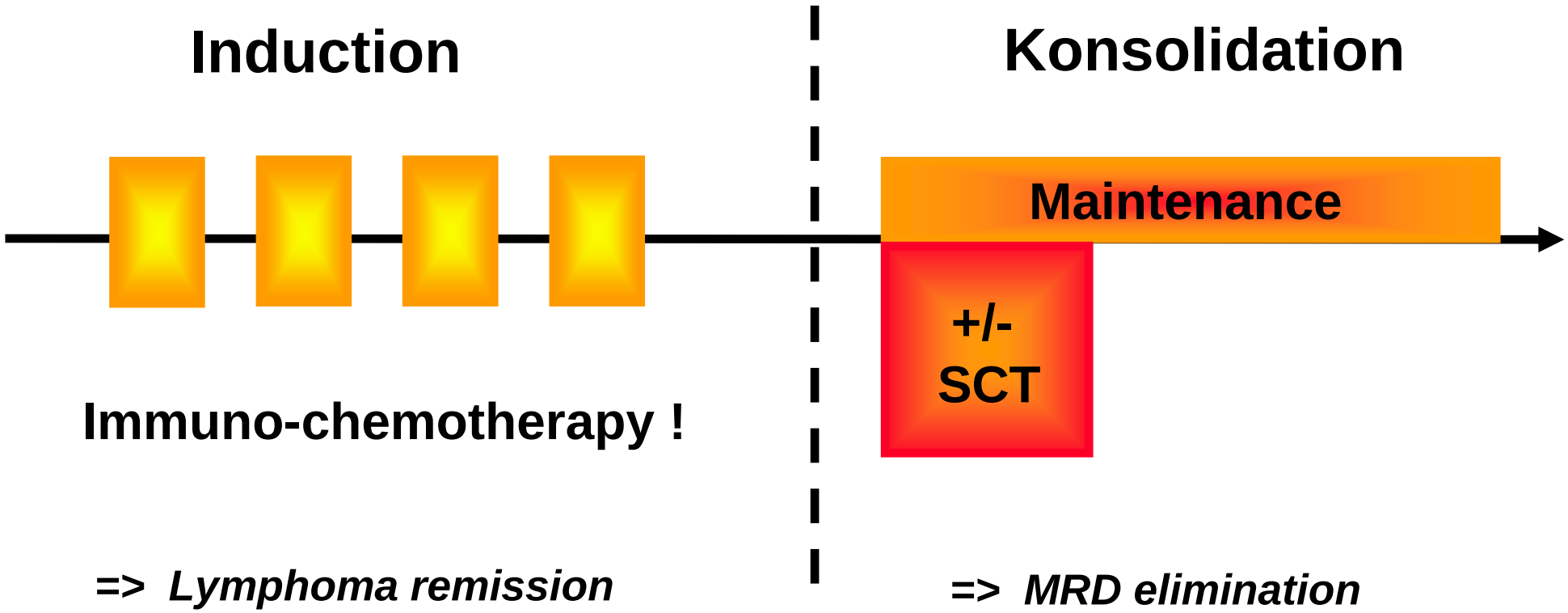
Overall Survival



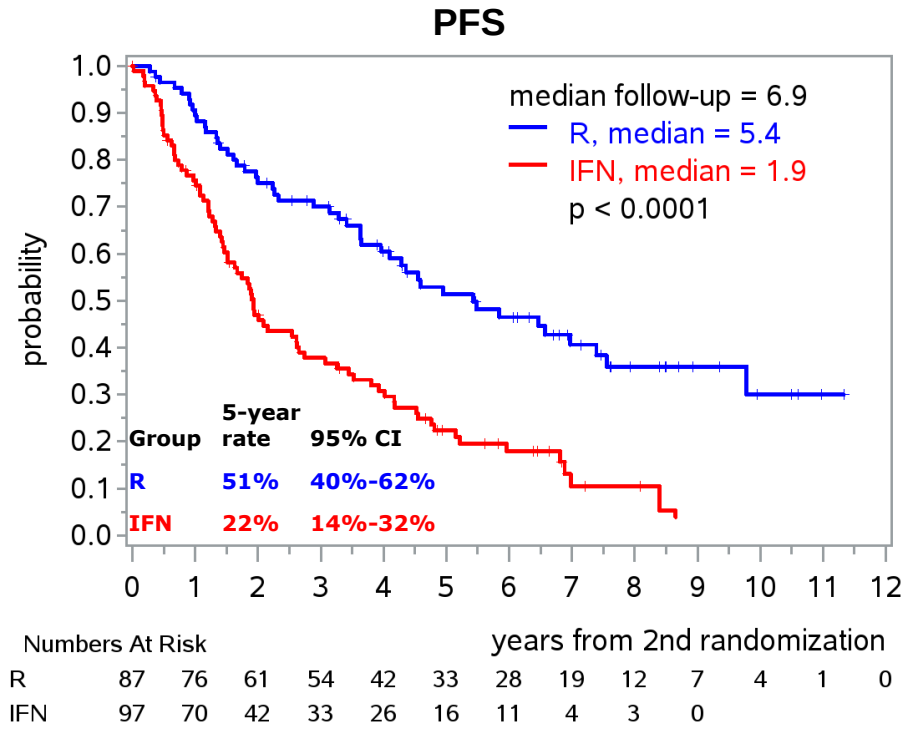
Median follow-up: approx. 80 months

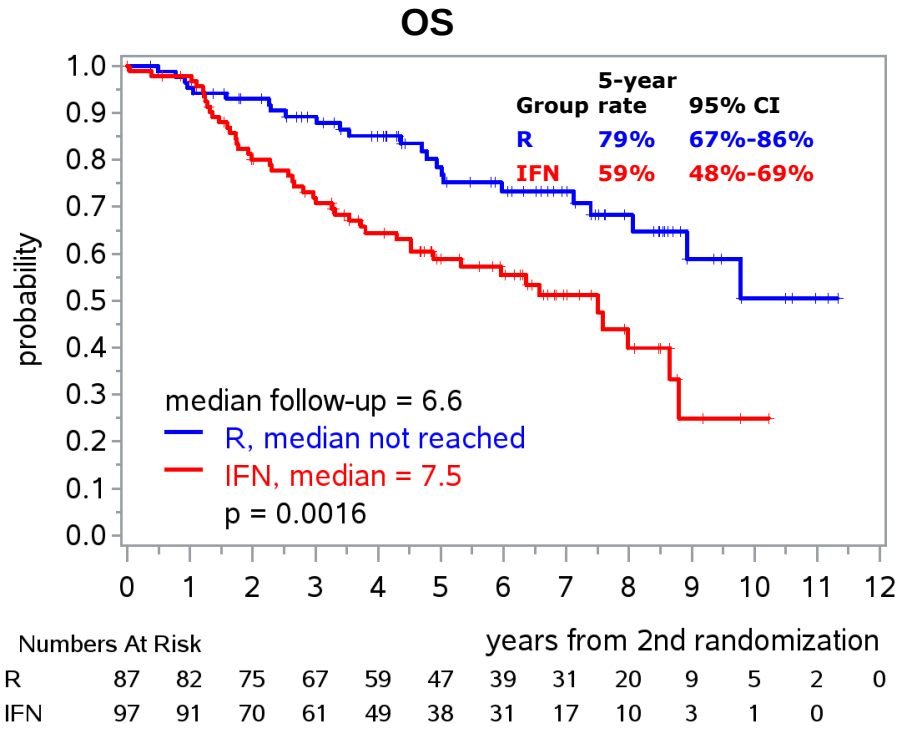
Robak, Lancet Oncol 2019

Optimal Therapy of MCL



R-CHOP +/- R maintenance

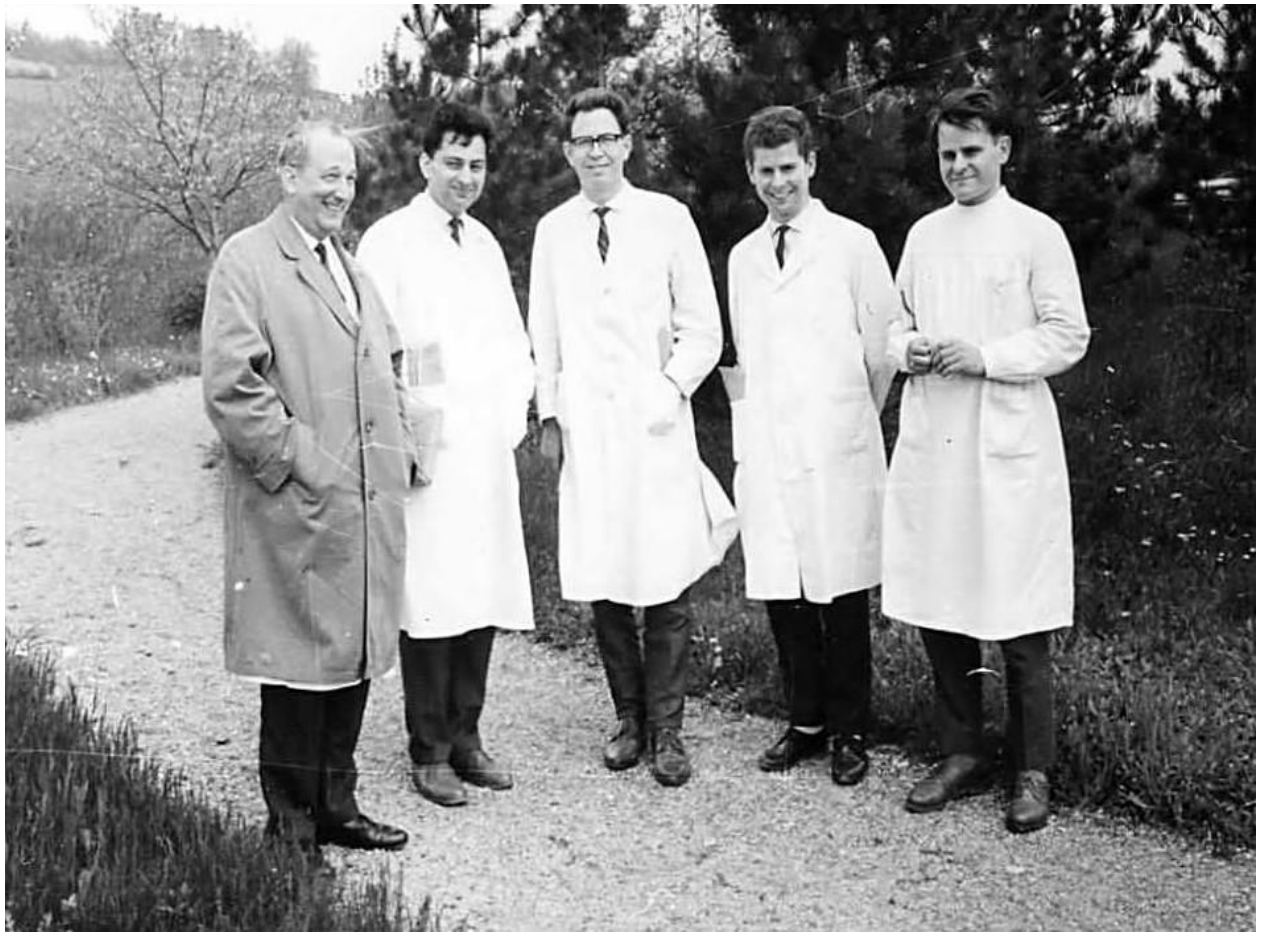




Kluin-Nelemans, 2020

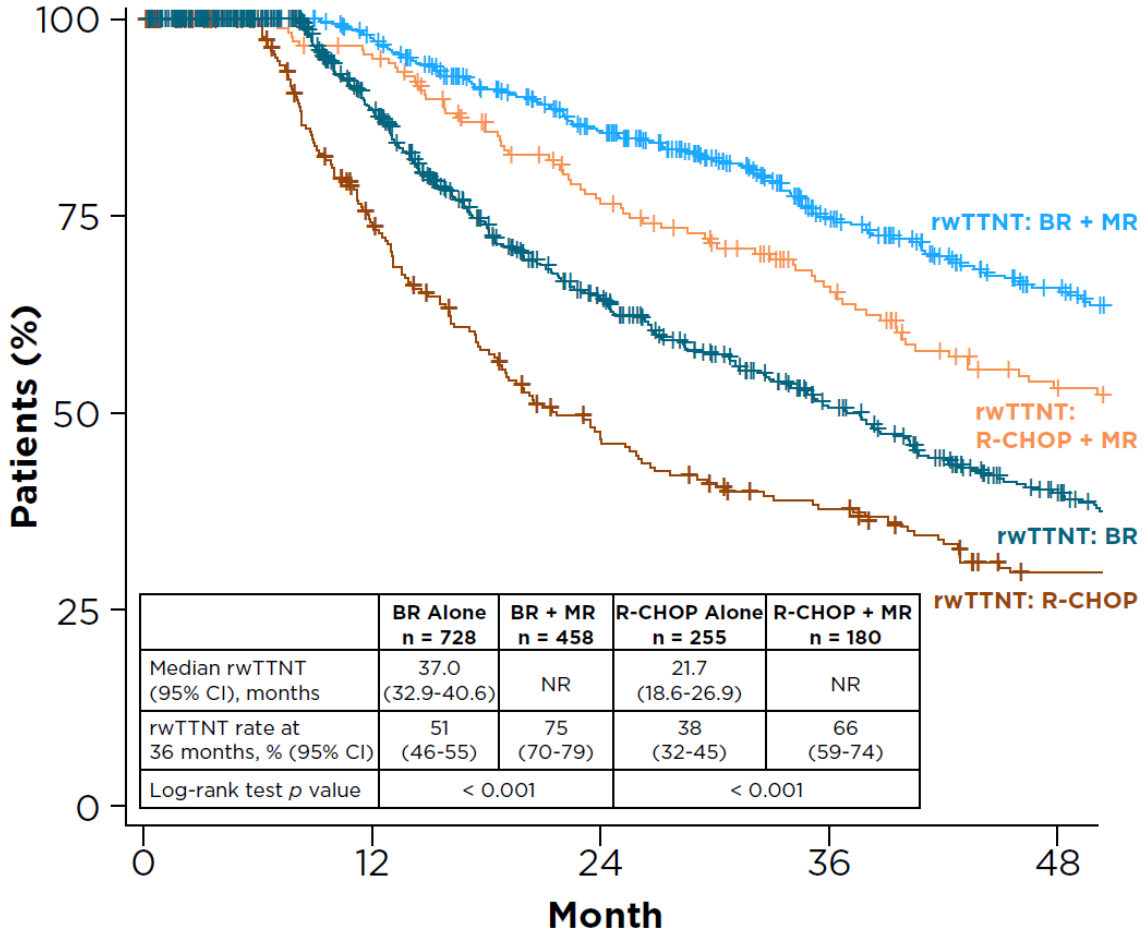
Bendamustine:

An ‘agent’ with a long history

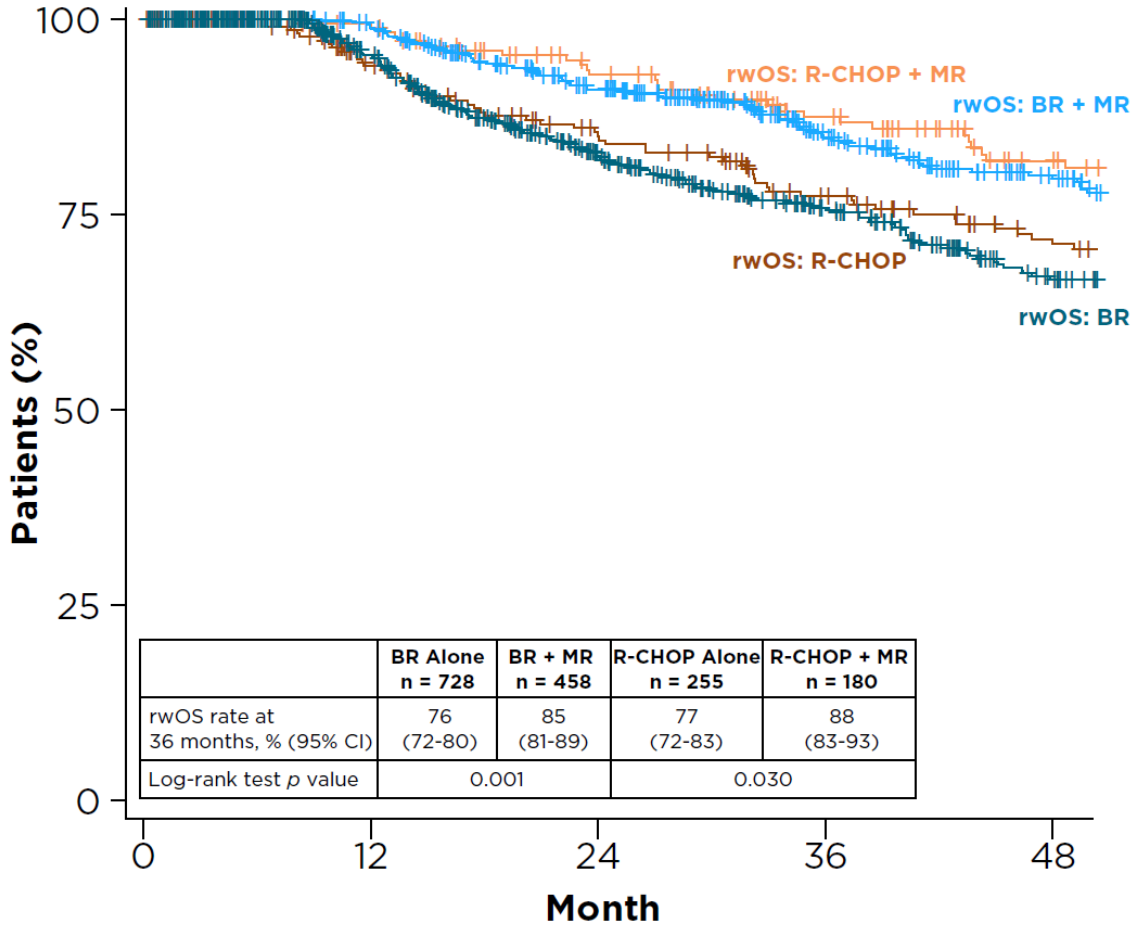


- **synthesis : W.Ozegowski, D.Krebs, Institute of Microbiology and Experimental Therapy, Jena (1962)**
- **Published in Journal für Praktische Chemie, Vol. 20, issue 3-4, 1963**

ROLE OF MAINTENANCE RITUXIMAB AFTER FIRST-LINE BR OR R-CHOP IN MCL PATIENTS FROM A LARGE US REAL-WORLD COHORT



	BR Alone n = 728	BR + MR n = 458	R-CHOP Alone n = 255	R-CHOP + MR n = 180
Median rwTTNT (95% CI), months	37.0 (32.9-40.6)	NR	21.7 (18.6-26.9)	NR
rwTTNT rate at 36 months, % (95% CI)	51 (46-55)	75 (70-79)	38 (32-45)	66 (59-74)
Log-rank test *p* value	< 0.001		< 0.001	



	BR Alone n = 728	BR + MR n = 458	R-CHOP Alone n = 255	R-CHOP + MR n = 180
rwOS rate at 36 months, % (95% CI)	76 (72-80)	85 (81-89)	77 (72-83)	88 (83-93)
Log-rank test *p* value	0.001		0.030	

Salles, EHA 2021 (JCO 2023)

Mantle cell lymphoma
Therapeutic algorithm

LMU KLINIKUM

young patient (≤65)	elderly patient (>65)	compromised patient
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dose-intensified immuno-chemotherapy (R-CHOP, high dose Ara-C) ⇒ Autologous SCT ⇒ Rituximab maintenance	conventional immuno-chemotherapy (VR-CAP, R-CHOP,BR, R-BAC) ⇓ Rituximab maintenance	Best supportive care? R-Chlorambucil BR (dose-reduced) R-CVP
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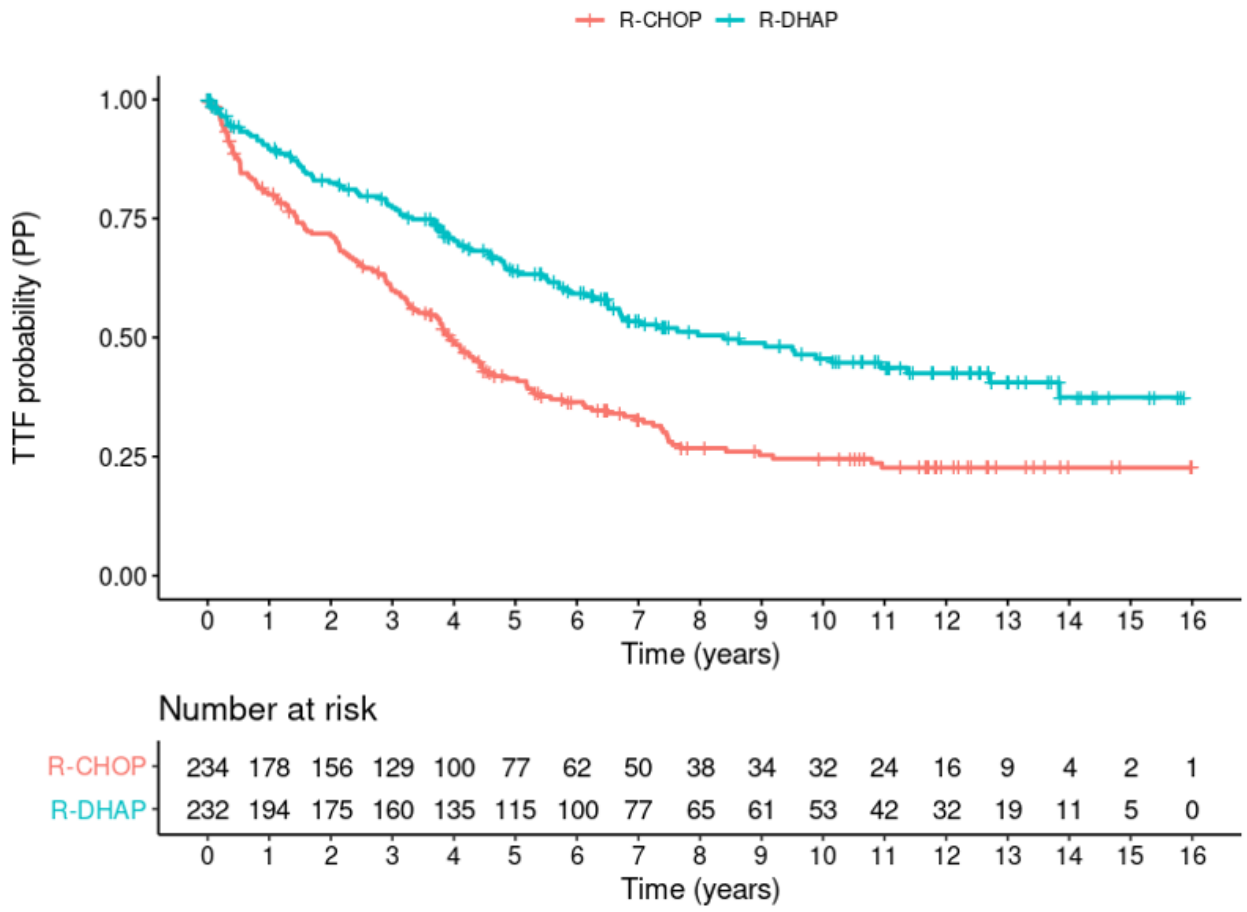
Targeted approaches: Ibrutinib, Lenalidomide, Temsirolimus, Bortezomib (preferable in combination) Alternatively: repeat previous therapy (long remissions)		

Dreyling, ESMO CR MCL 2017 (updated)

Updated Results 2021 – TTF (PP)



- Median follow-up 10.6 years
- Median TTF:

  R-CHOP 3.9 years

  R-DHAP 8.4 years
- 10-year TTF (95% CI):

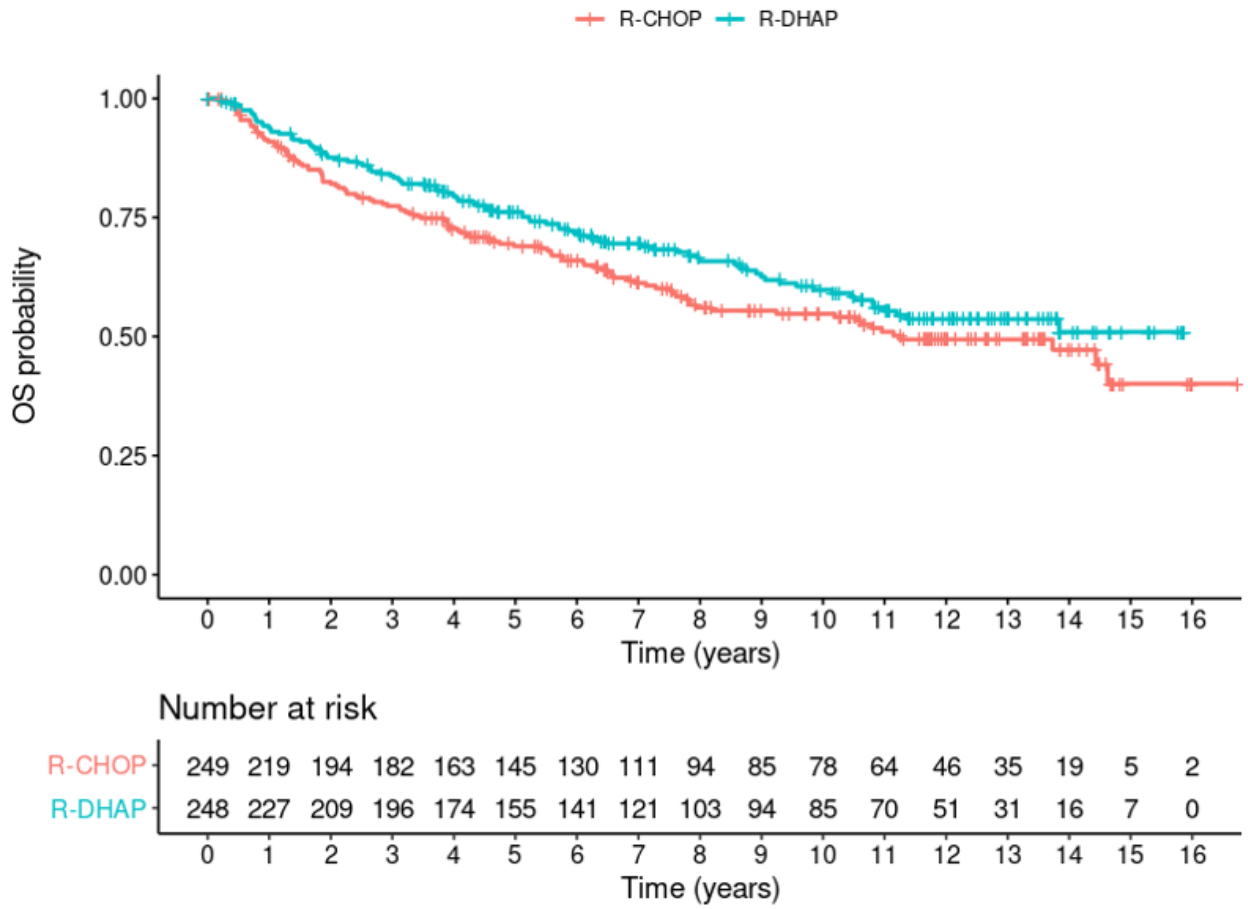
  R-CHOP 25% (19% - 32%)

  R-DHAP 46% (39% - 54%)
- Overrunning analysis (adjusted for interim analyses):

  Hazard ratio 0.59 (p=0.038)

Hermine, ASH 2021, #380, JCO 2022

Updated Results 2021 – Overall Survival



- Median follow-up 11.0 years
- Median OS:

  R-CHOP 11.3 years

  R-DHAP not reached

  p=0.12
- 10-year OS (95% CI):

  R-CHOP 55% (48% - 62%)

  R-DHAP 60% (53% - 67%)
- Hazard Ratio 0.80 (0.61-1.06), p=0.12

  MIPI-adjusted Hazard ratio 0.74 (0.56-0.98), p=0.038

  MIPI and Ki-67-adjusted hazard ratio (N=297):

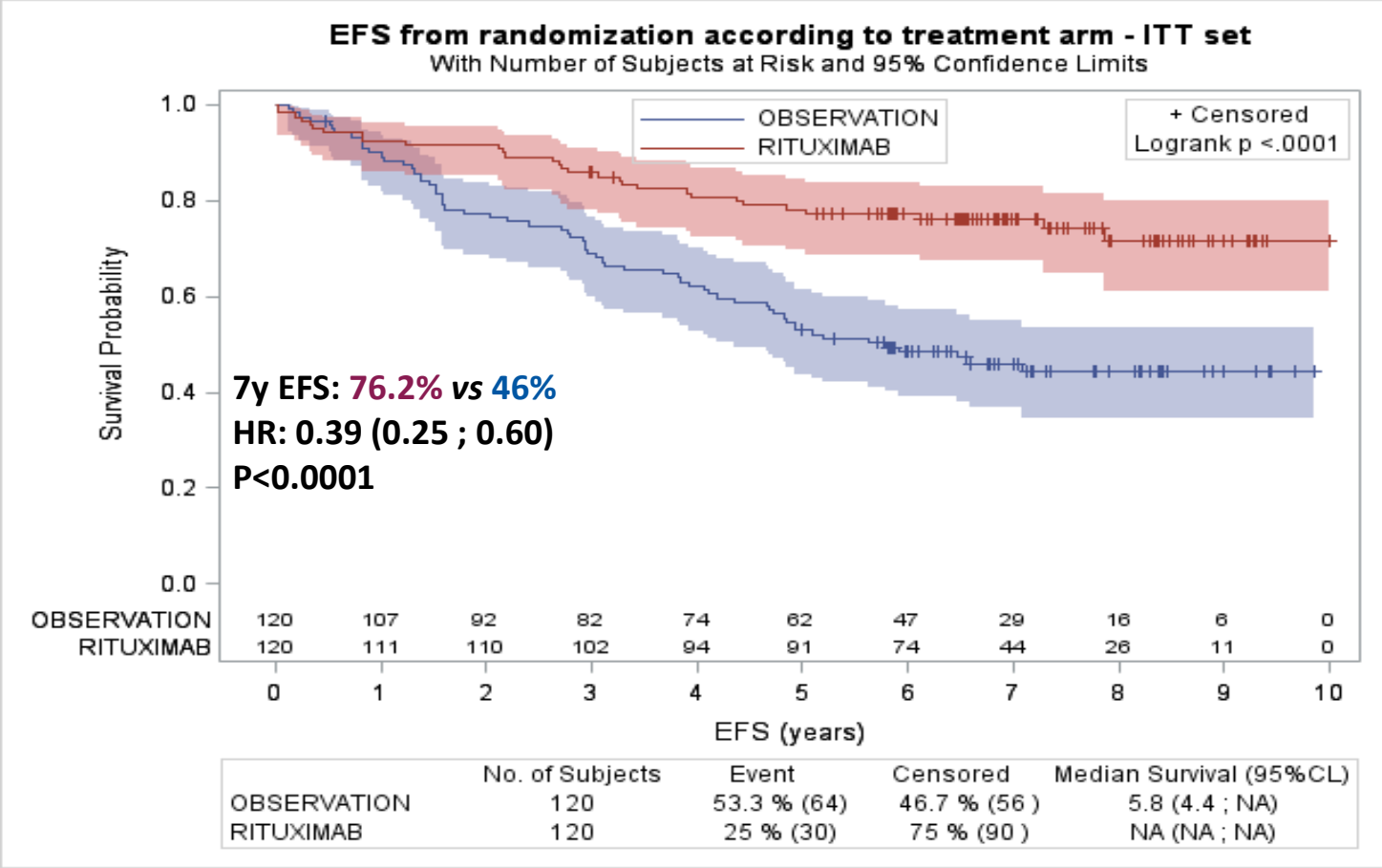
  0.60 (0.41-0.87), p=0.0066

Hermine, ASH 2021, #380, JCO 2022

EFS from randomization

Median FU for living patients:

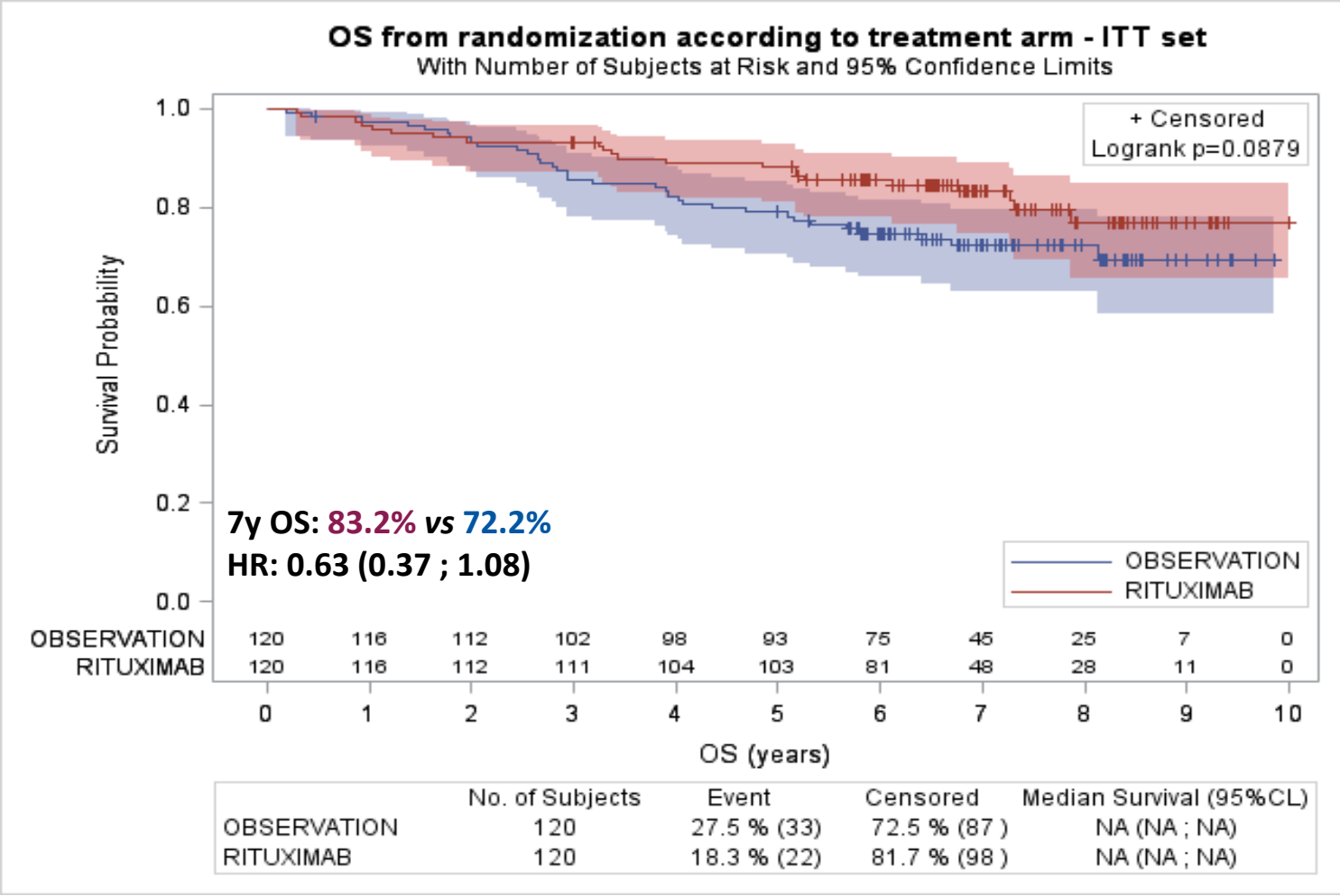
- **from inclusion: 7.5 y (95% CI 7.4-7.7)**
- **from randomization: 7 y (95% CI 6.8-7.2)**



Nature of first Event	Observation, N=64/120 (53%)	Rituximab N=30/120 (25%)
Relapse	51 (80%)	19 (63%)
Death w/o relapse	9 (14%)	6 (20%)
Serious infections	4 (6%)	4 (13%)
Life threatening allergy to R	0	1 (4%)

Sarkozy, ICML: # 100

Overall Survival from randomization



Cause of death	Observation, N=33/120 (27.5%)	Rituximab, N=22/120 (18%)
Lymphoma	16 (48.5%)	11 (50%)
Secondary Malignancies	6 (18%)	7 (32%)
Treatment related: infectious	3 (9%)	1 (5%)
Vascular event	2 (6%)	0 (0%)
Treatment related during allotransplant	2 (6%)	2 (9%)
Other	2 (6%)**	1 (4%)*
Unknown	2 (6%)	0

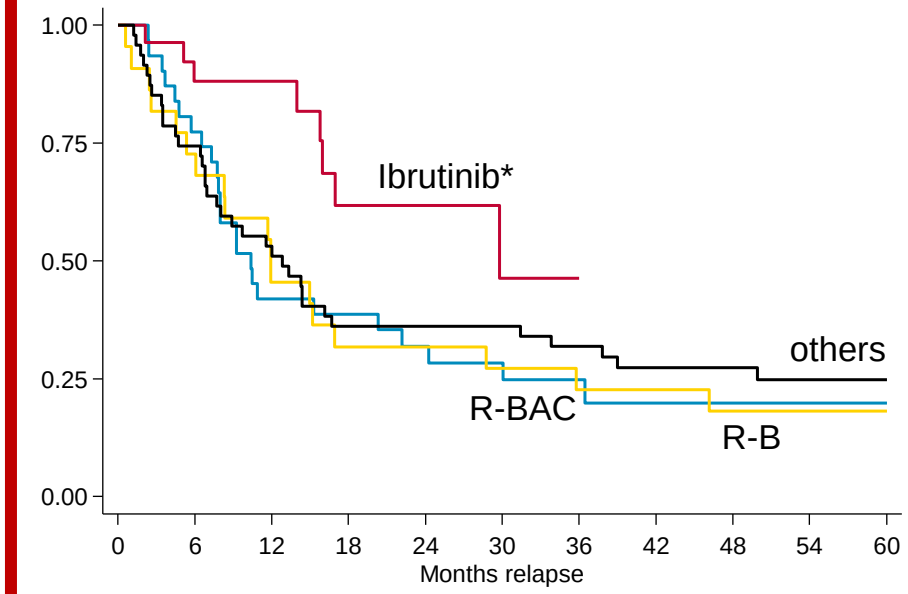
*Suicide, **acute respiratory destress, car accident,

Sarkozy, ICML: # 100

Ibrutinib in relapsed MCL (POD 24)

Overall survival

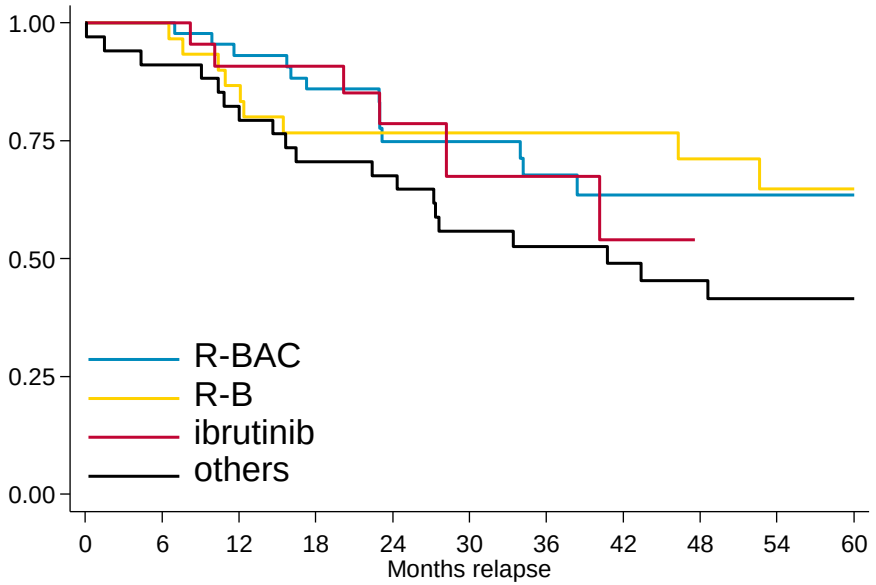
Early POD



At risk:											
BAC	31	24	13	12	9	8	5	4	3	3	3
BR	22	16	10	7	7	6	5	5	4	3	2
ibru	27	21	16	8	5	3	0	0	0	0	0
other	47	35	24	17	17	17	15	11	11	10	6

*Ibru vs R-B and R-BAC (P=0.02); vs others (P=0.03)

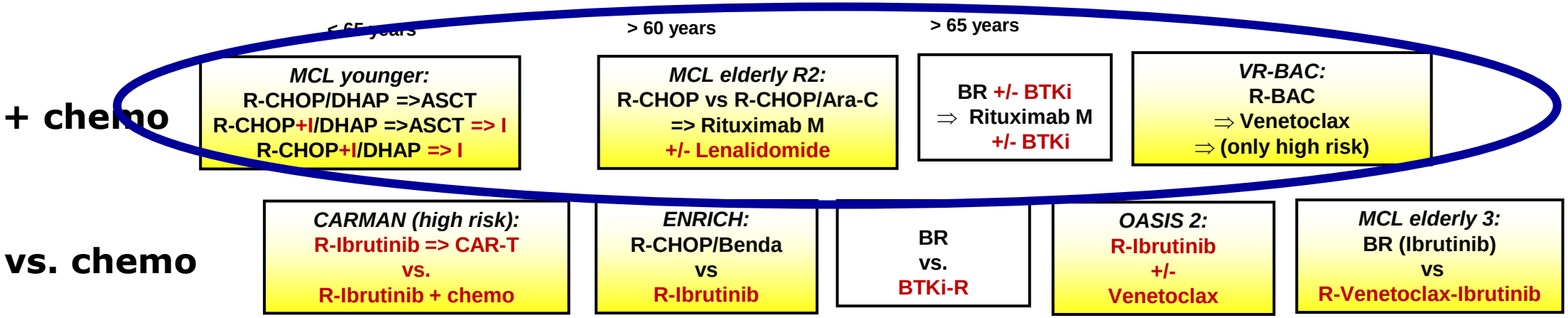
Late-POD



At risk:											
BAC	45	45	40	35	26	23	16	14	12	8	7
BR	32	30	26	23	22	20	16	15	13	10	9
ibru	23	22	20	18	10	6	6	4	0	0	0
other	34	31	27	24	23	19	16	13	12	8	7

Visco, Leukemia 2021

European MCL Network
Study generation 2023

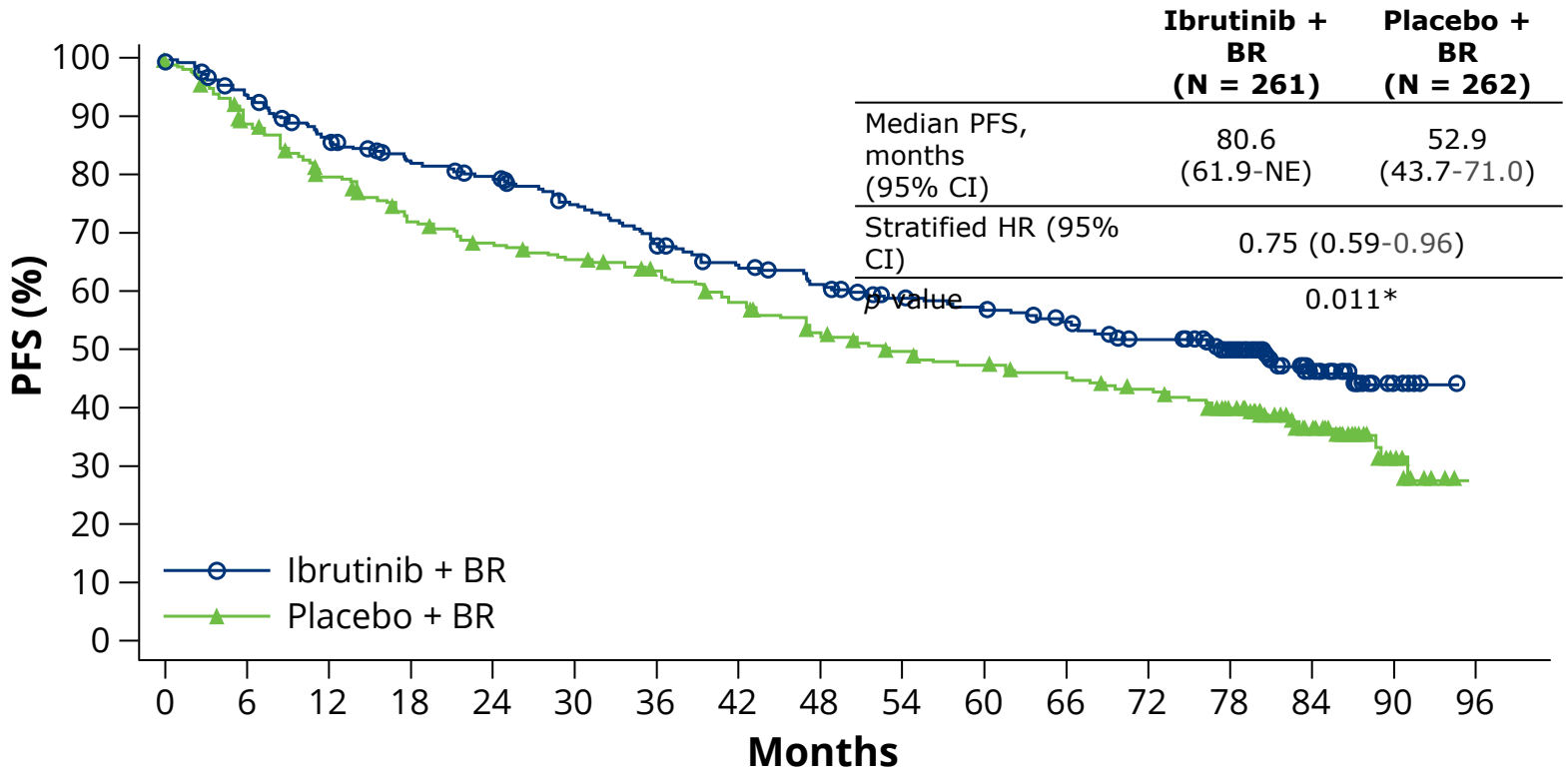


Relapse

Mantle cell Lymphoma (older patients)

BR +/- Ibrutinib

Wang, NEJM 2022



	Ibrutinib + BR (N = 261)	Placebo + BR (N = 262)
Median PFS, months (95% CI)	80.6 (61.9-NE)	52.9 (43.7-71.0)
Stratified HR (95% CI)	0.75 (0.59-0.96)	
p-value	0.011*	

Patients at Risk

Ibrutinib + BR	261	228	207	191	182	167	152	139	130	120	115	106	95	78	39	11	0
Placebo + BR	262	226	199	177	166	158	148	135	119	109	103	98	90	78	41	11	0

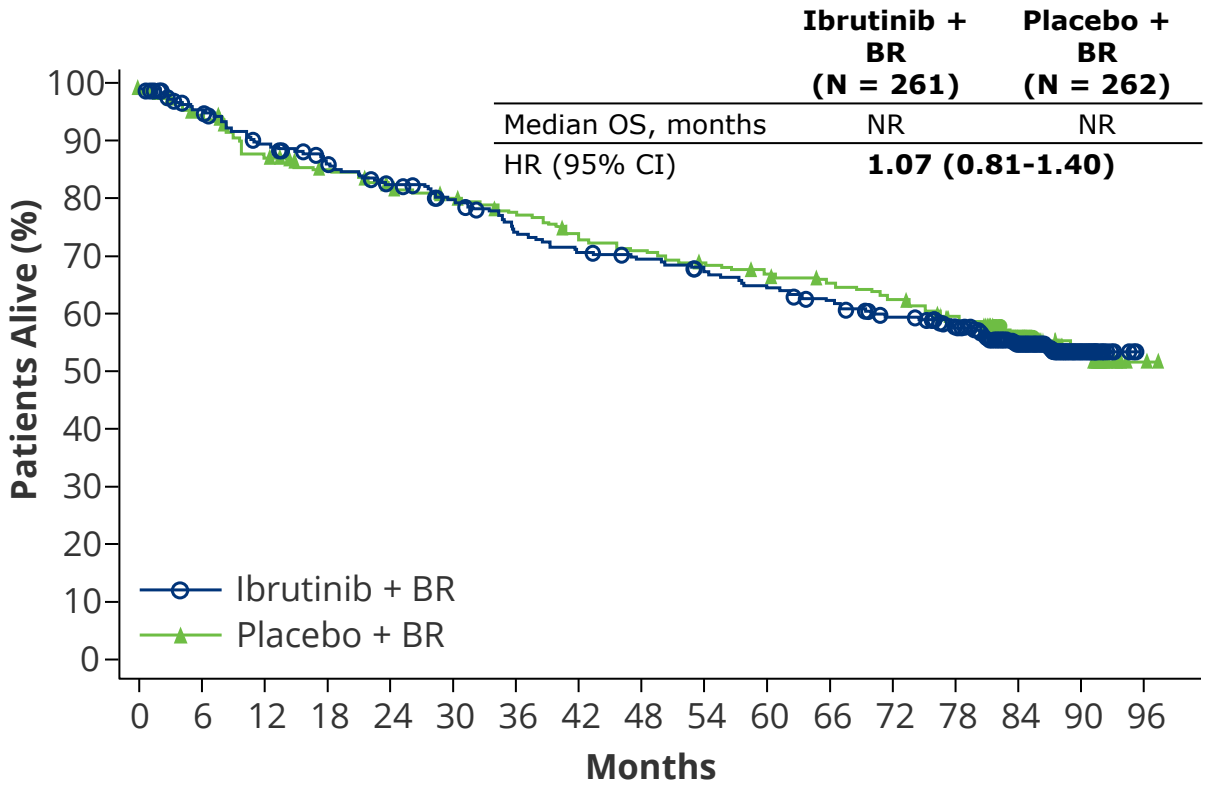
Ibrutinib + BR and R maintenance achieved:

- Significant improvement in median PFS by 2.3 years (6.7 vs 4.4 years)
- 25% reduction in risk of PD or death

Mantle cell Lymphoma (older patients)

BR +/- Ibrutinib

Wang, NEJM 2022



Patients at Risk

Ibrutinib + BR	261	239	221	208	197	187	171	163	158	152	145	138	128	118	70	25	0
Placebo + BR	262	244	223	212	203	197	188	177	171	165	159	154	147	137	90	31	2

Cause of death	Ibrutinib + BR (N = 261)	Placebo + BR (N = 262)
Death due to PD and TEAE	**58 (22.2%)**	**70 (26.7%)**
Death due to PD	**30 (11.5%)**	**54 (20.6%)**
Death due to TEAEs*	**28 (10.7%)**	**16 (6.1%)**
Death during post-treatment follow-up excluding PD and TEAEs	**46 (17.6%)**	**37 (14.1%)**
Total deaths	**104 (39.8%)**	**107 (40.8%)**

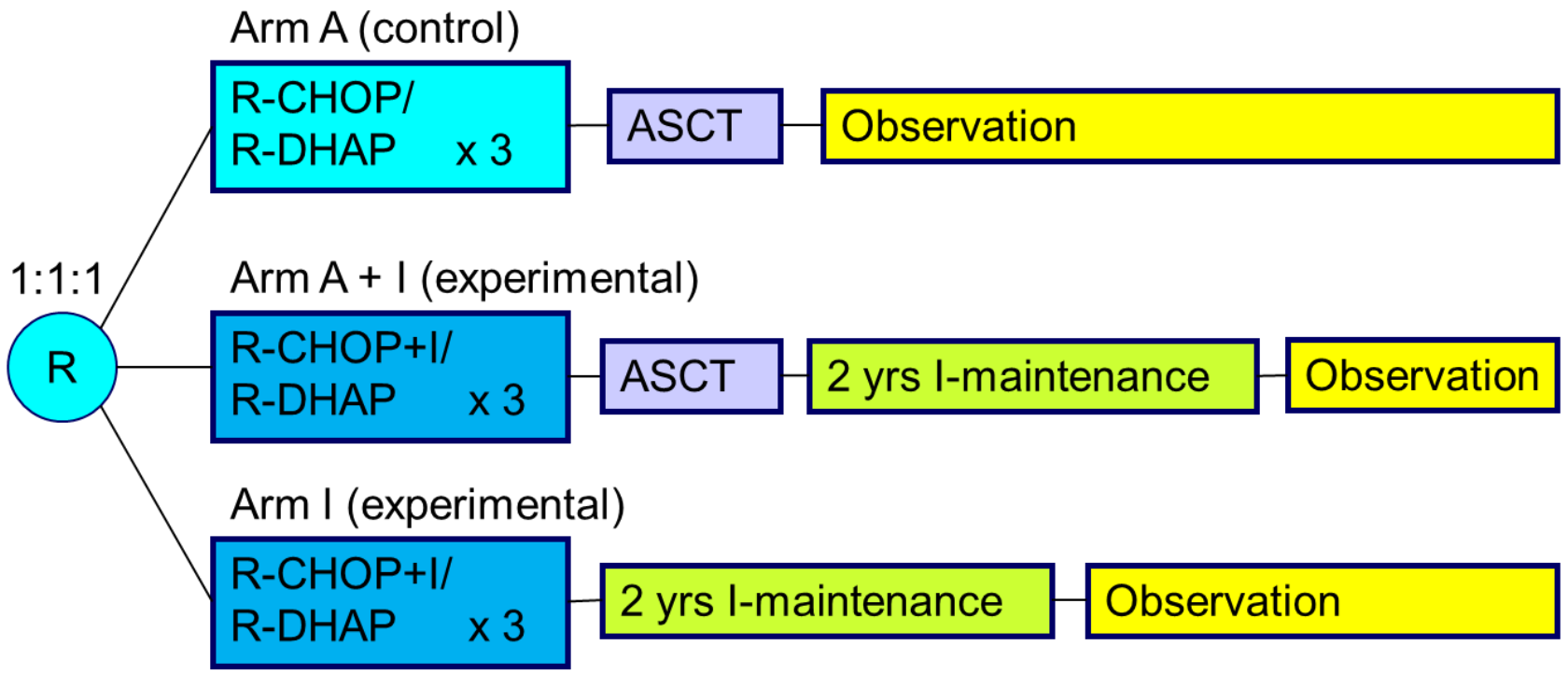
- Death due to Covid-19: 3 patients in the ibrutinib arm during the TEAE period and 2 patients in the placebo arm after the TEAE period
- Exploratory analysis of cause-specific survival including only deaths due to PD or TEAEs showed an HR of 0.88

TRIANGLE: Trial Design

- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2

- Primary outcome: FFS

- Secondary outcomes:
  - Response rates
  - PFS, RD
  - OS
  - Safety



- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.

Dreyling, ASH 2022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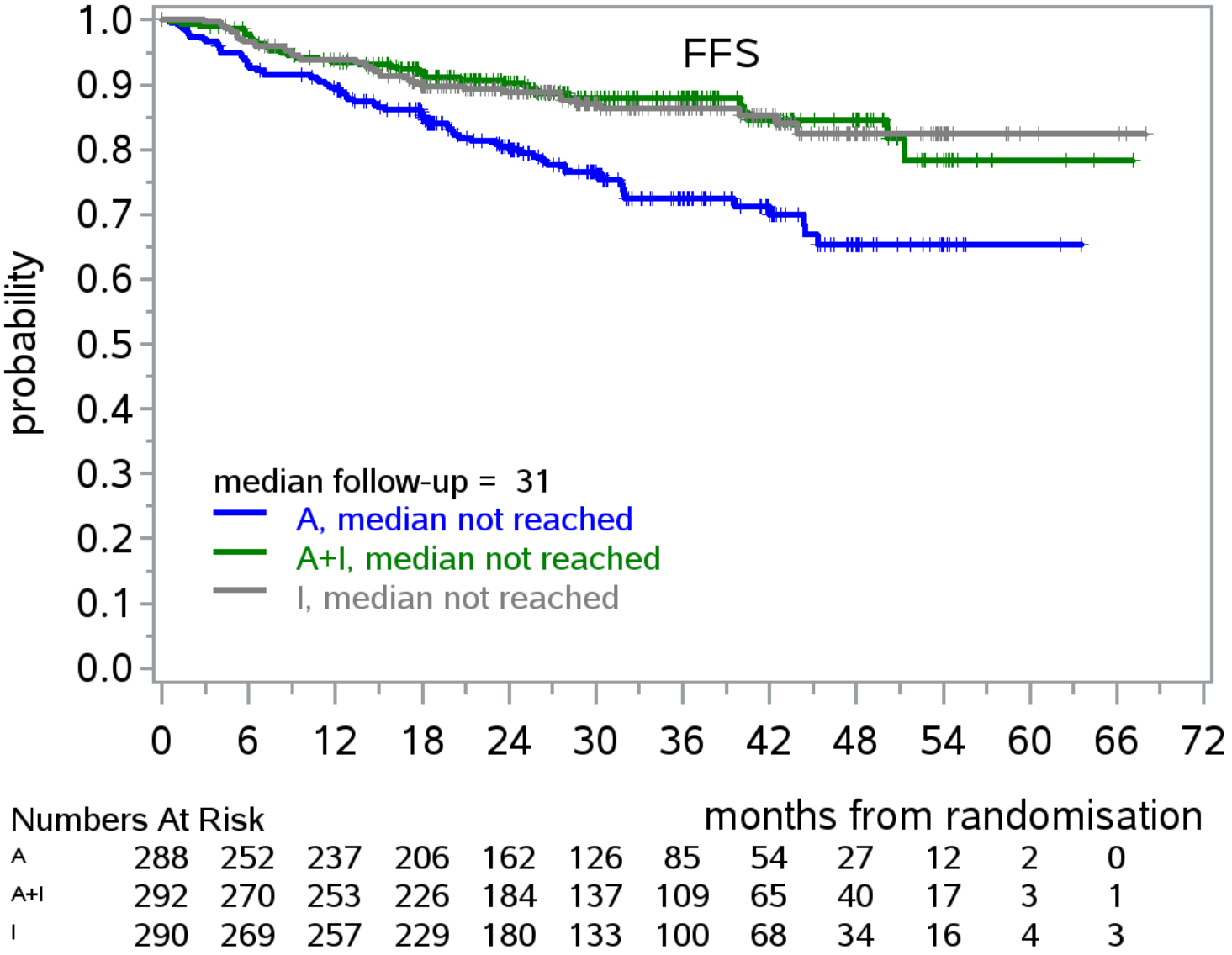
TRIANGLE: FFS Superiority of A+I vs. I ?



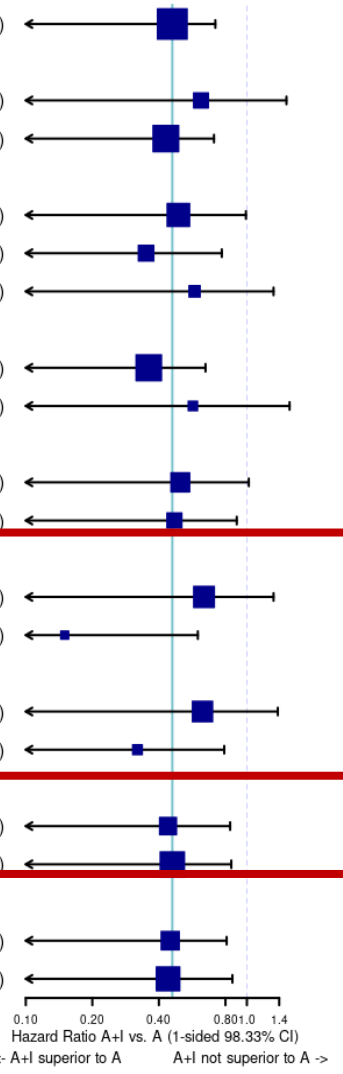
- Test A+I vs. I ongoing, no decision yet

Next lymphoma treatment (among patients with first treatment failure)	A (n=68)		A+I (n=35)		I (n=37)	
Treatment with Ibrutinib	34	79%	4	24%	3	11 %
Treatment without Ibrutinib	9	21%	13	76%	24	89 %
No treatment	25		18		10	

A+I arm: IR-CHOP/R-DHAP+ASCT+I; I arm: IR-CHOP/R-DHAP+I. I: ibrutinib

TRIANGLE: FFS Superiority of A+I vs. A

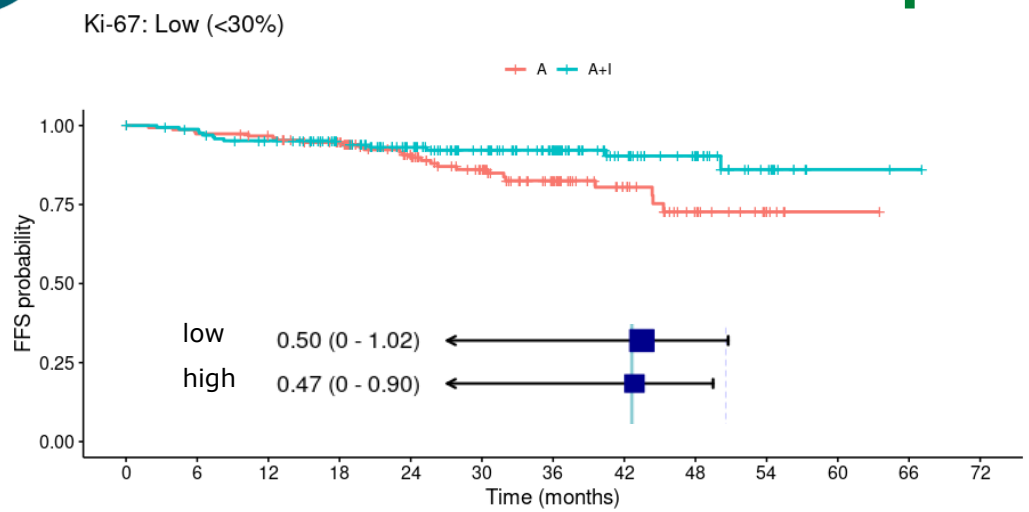
Subgroup (interaction p-value)	No. of patients	No. of events	Hazard ratio (1-sided 98.33% CI)
All	580	103	0.46 (0 - 0.72)
Sex (p=0.0016)			
Female	146	23	0.62 (0 - 1.51)
Male	434	80	0.43 (0 - 0.71)
MIPI			
Low	336	40	0.49 (0 - 0.99)
Intermediate (p=0.49)	159	35	0.35 (0 - 0.77)
High (p=0.69)	85	28	0.58 (0 - 1.32)
Cytology (p=0.48)			
Non-blastoid	426	68	0.36 (0 - 0.65)
Blastoid	60	18	0.57 (0 - 1.56)
Ki-67 (p=0.82)			
Low	234	39	0.50 (0 - 1.02)
High	150	38	0.47 (0 - 0.90)
P53 expression (p=0.039)			
Low	284	36	0.64 (0 - 1.32)
High	44	16	0.15 (0 - 0.60)
High risk biology (p=0.19)			
Low	270	31	0.63 (0 - 1.38)
High	64	25	0.32 (0 - 0.79)
R maintenance ITT (p=0.96)			
No	191	48	0.44 (0 - 0.84)
Yes	389	55	0.46 (0 - 0.85)
R maintenance mAT (p=0.94)			
No	217	55	0.45 (0 - 0.81)
Yes	363	48	0.44 (0 - 0.86)

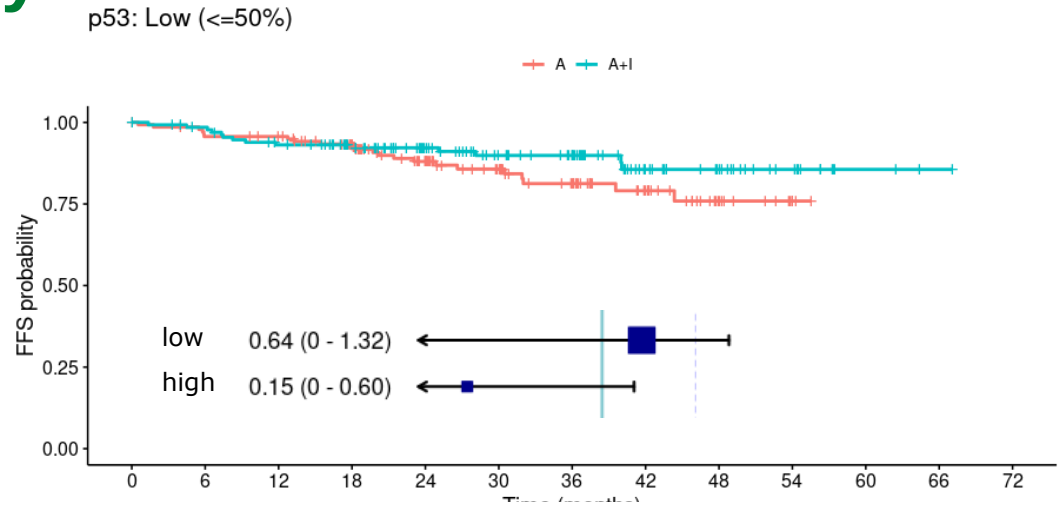


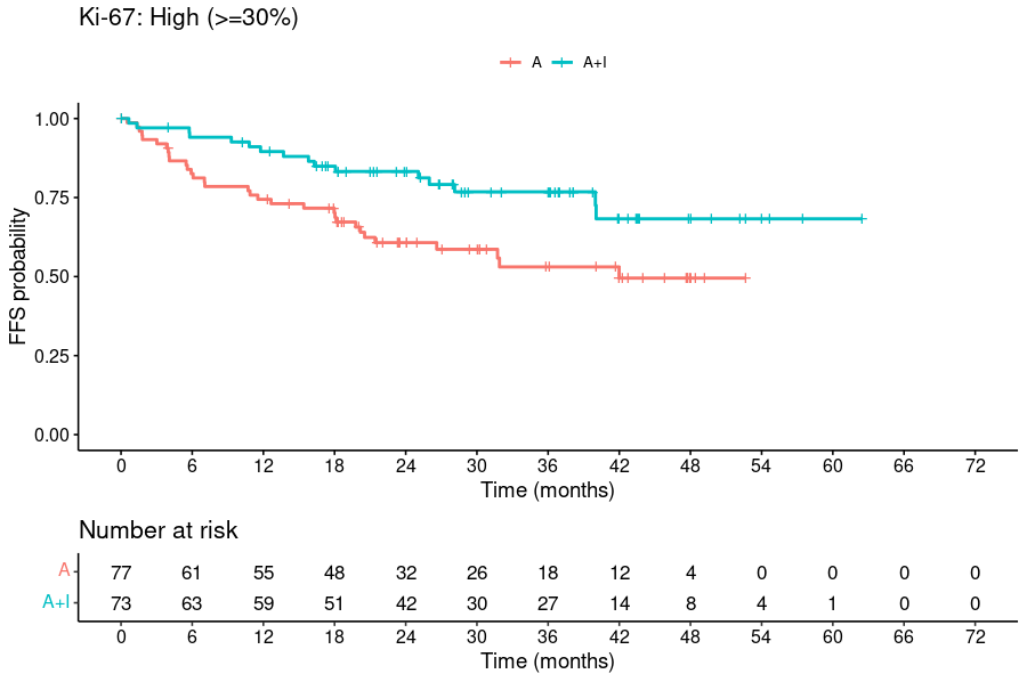
- similar in all MIPI groups
- No differential efficacy according to cytology and Ki-67
- More effective in high p53 expressors
- Trend toward higher efficacy in high risk biology
- No differential efficacy by rituximab maintenance

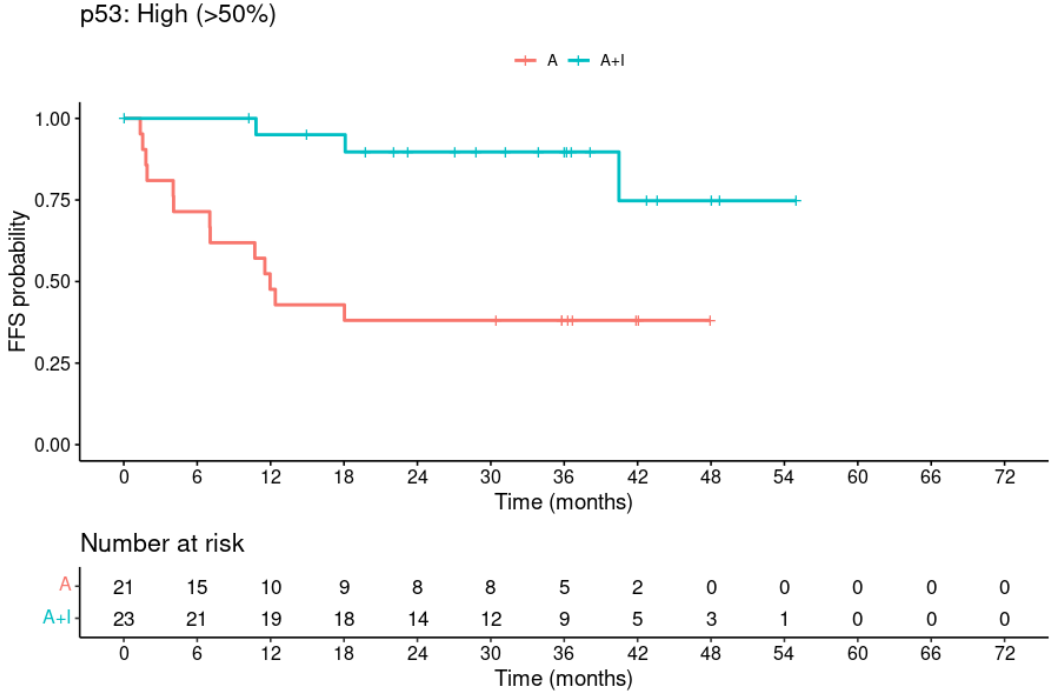
A arm: R-CHOP/R-DHAP+ASCT; A+I arm: IR-CHOP/R-DHAP+ASCT+I

TRIANGLE: FFS Superiority of A+I vs. A







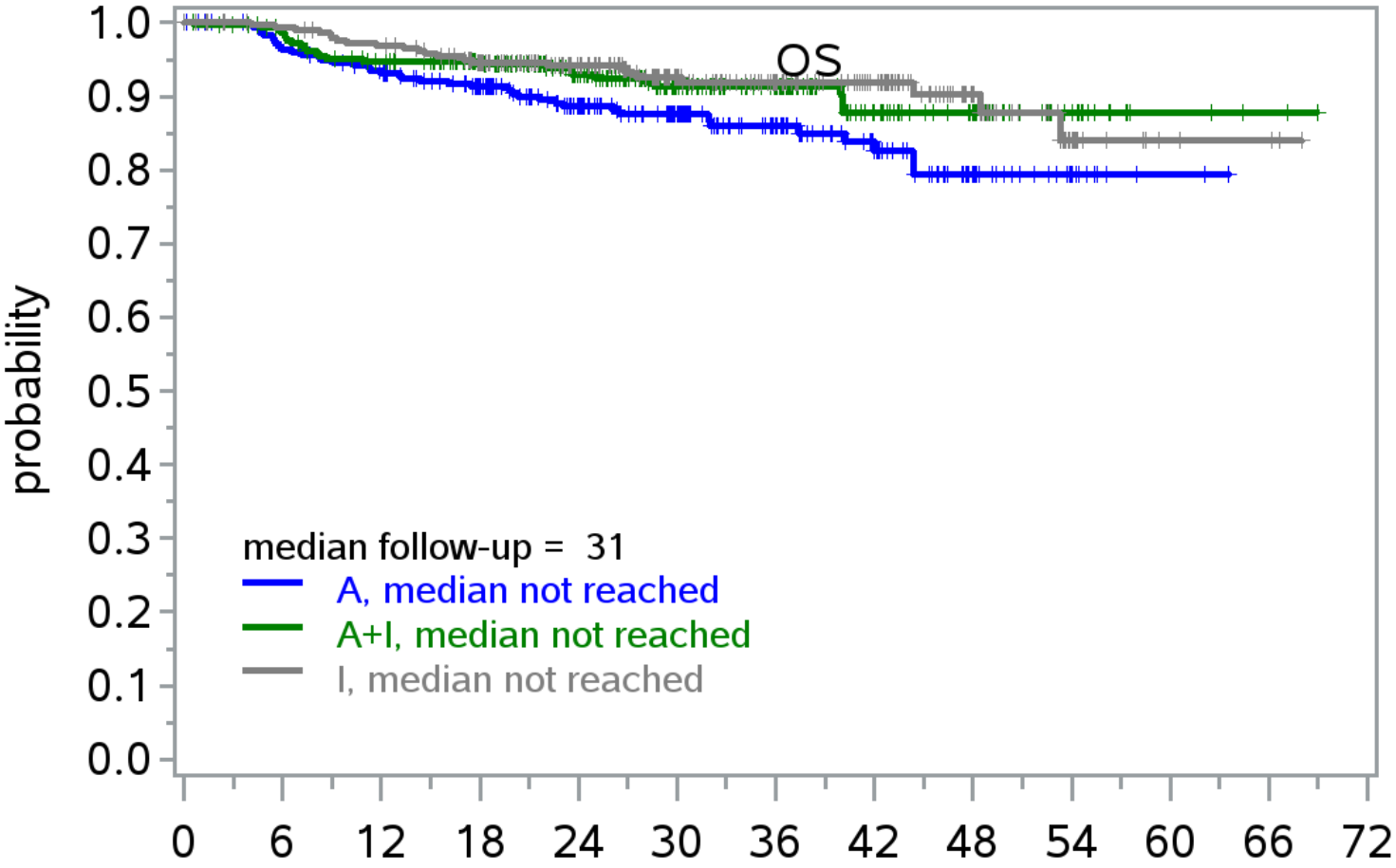


A arm: R-CHOP/R-DHAP+ASCT; A+I arm: IR-CHOP/R-DHAP+ASCT+I

Mantle cell Lymphoma

MCL younger +/- Ibrutinib

Dreyling, ASH 2022, #1



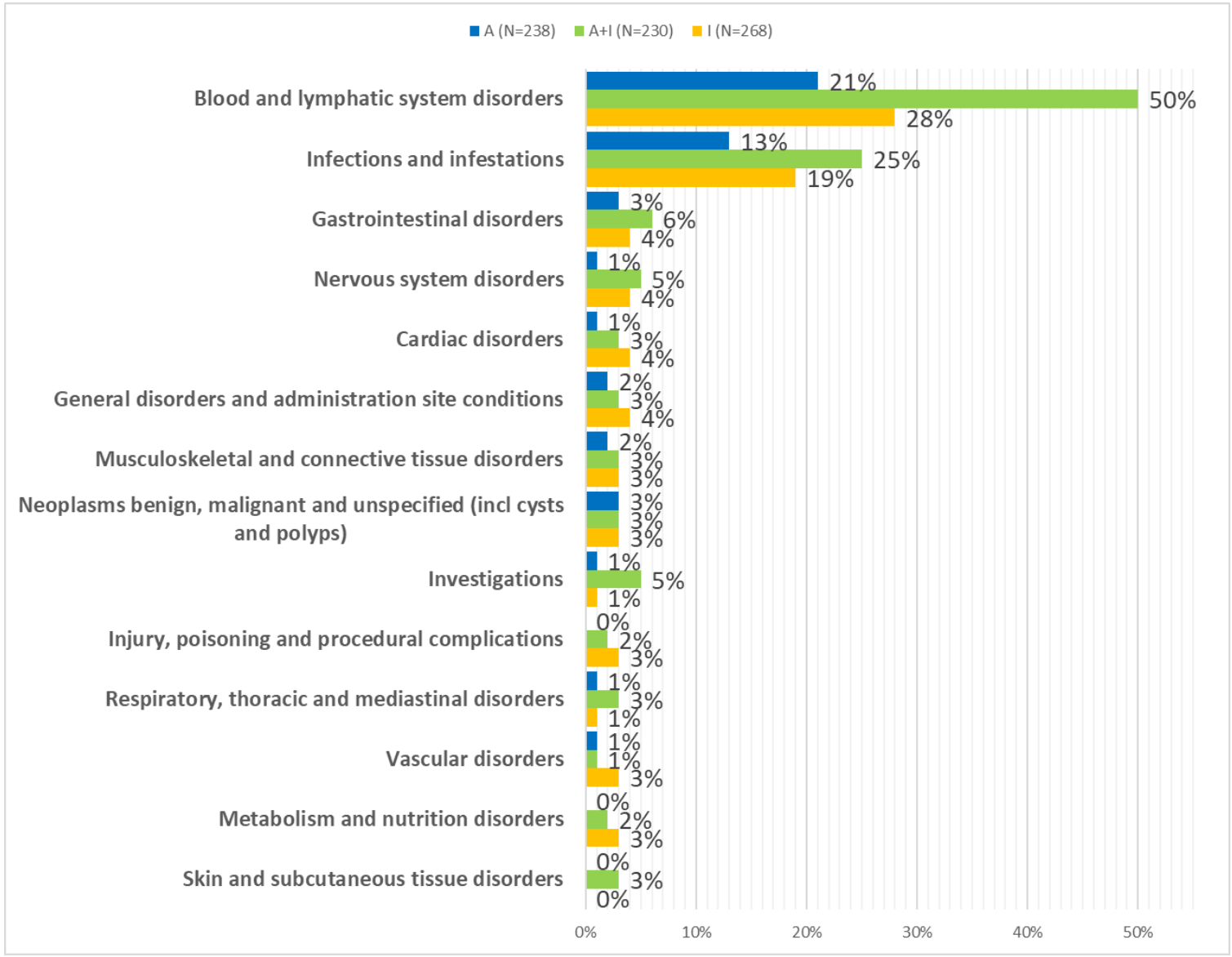
Numbers At Risk

A	288	270	256	230	181	145	97	63	32	15	2	0
A+I	292	280	262	238	195	142	113	67	42	19	4	2
I	290	281	272	248	197	145	109	77	38	16	4	3

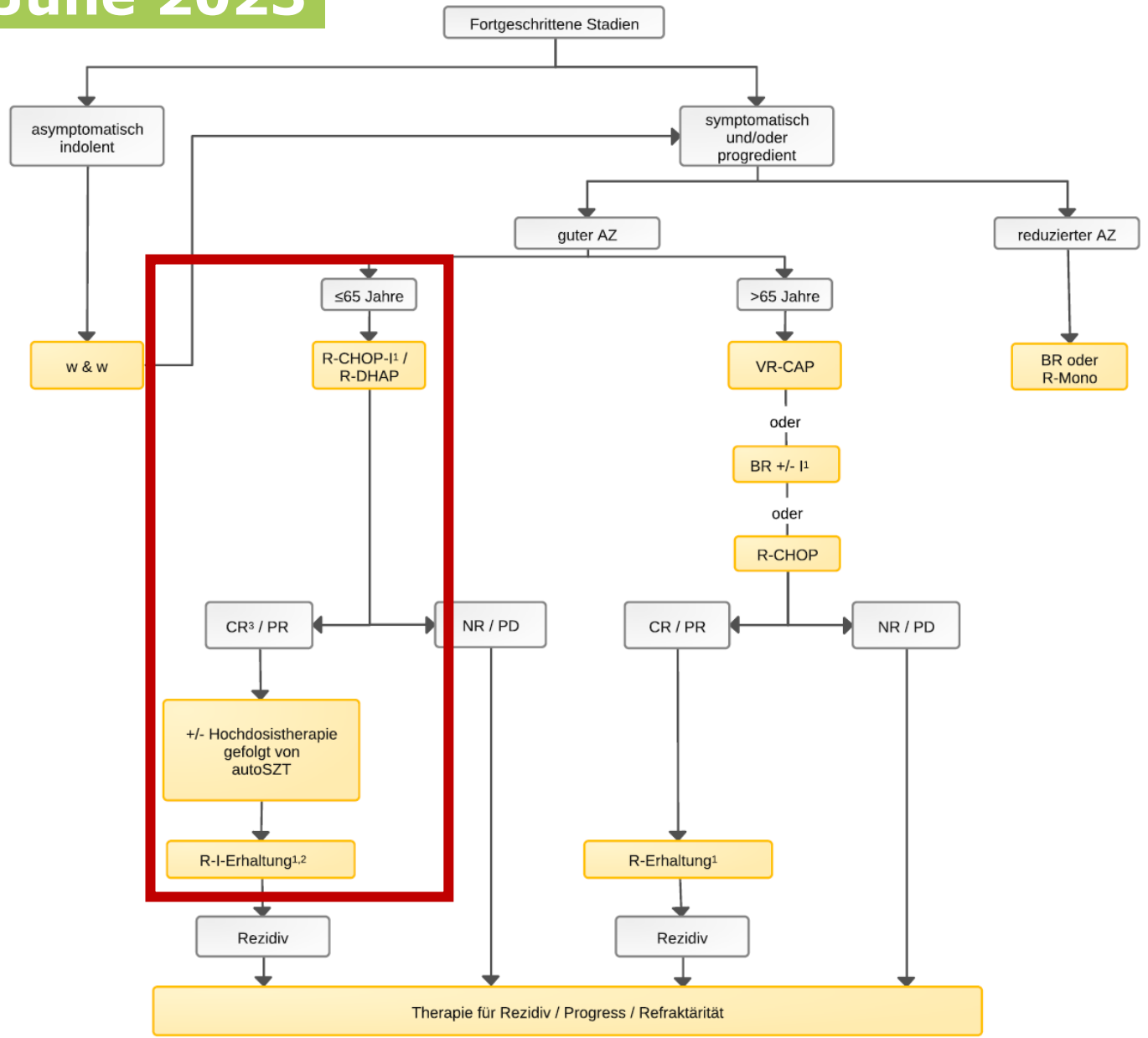
Mantle cell Lymphoma

MCL younger +/- Ibrutinib

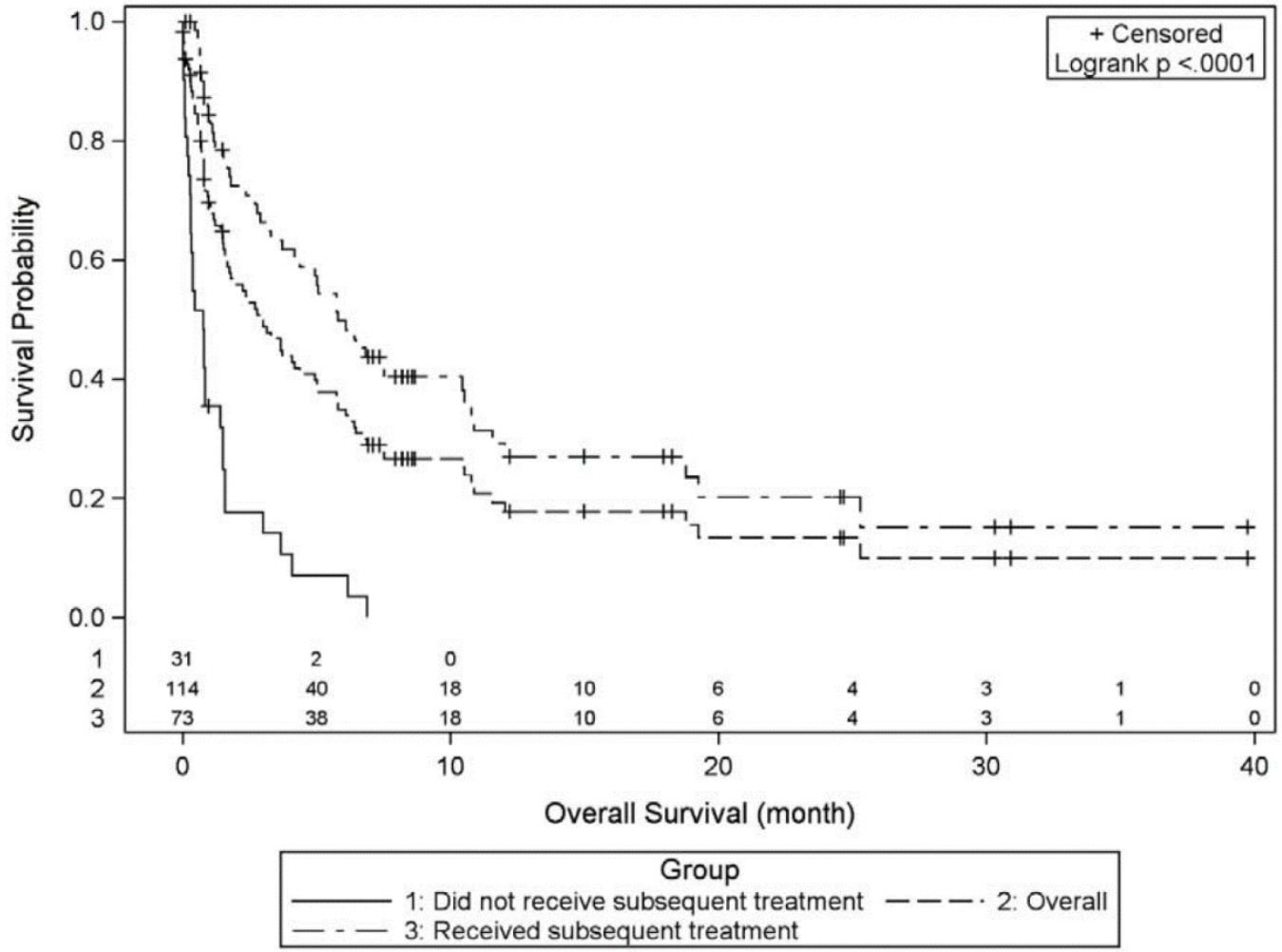
Dreyling, ASH 2022, #1



Mantle cell Lymphoma
Onkopedia June 2023



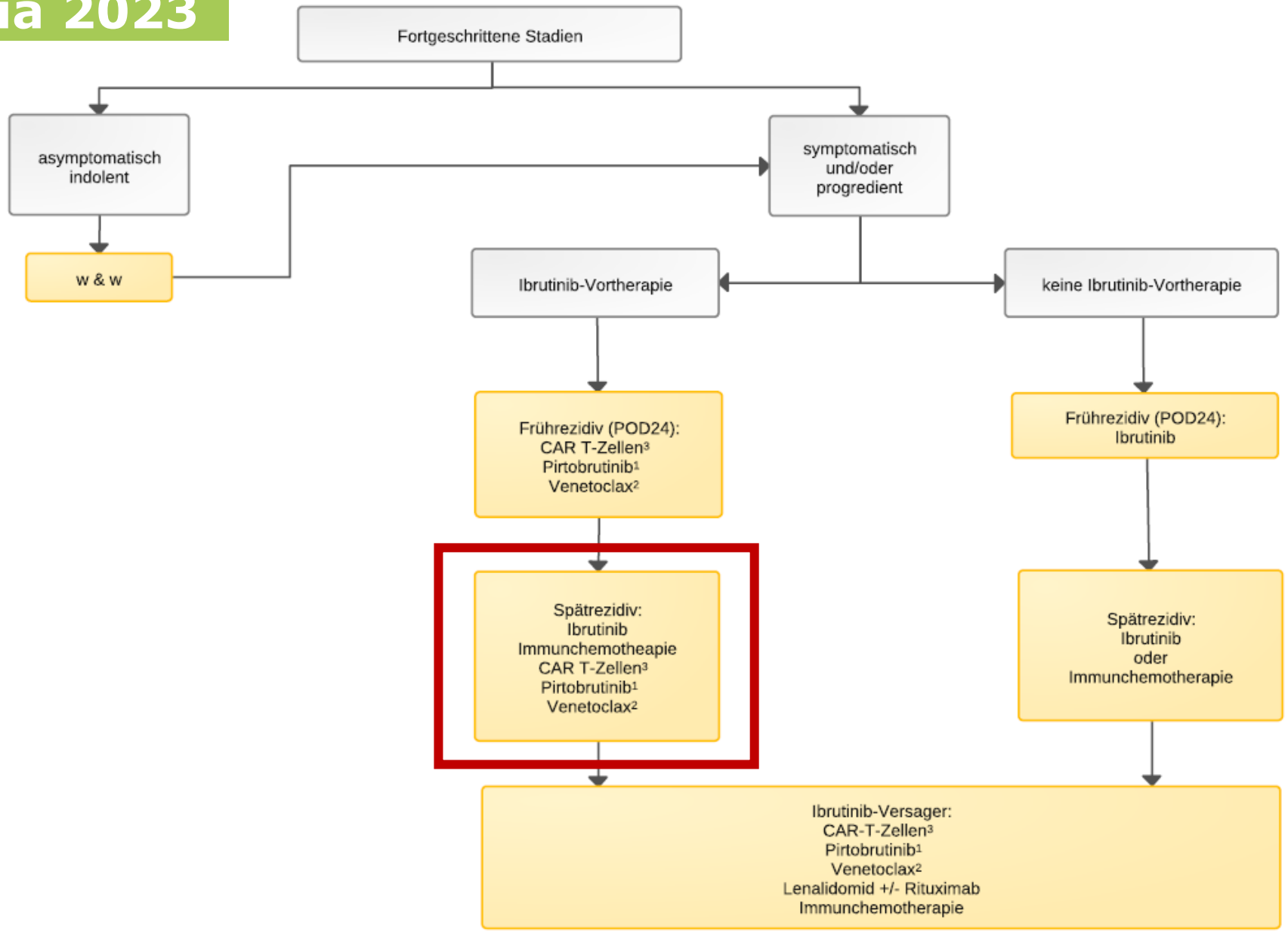
Relapsed mantle cell lymphoma
Failure under ibrutinib



Martin, Blood 2016

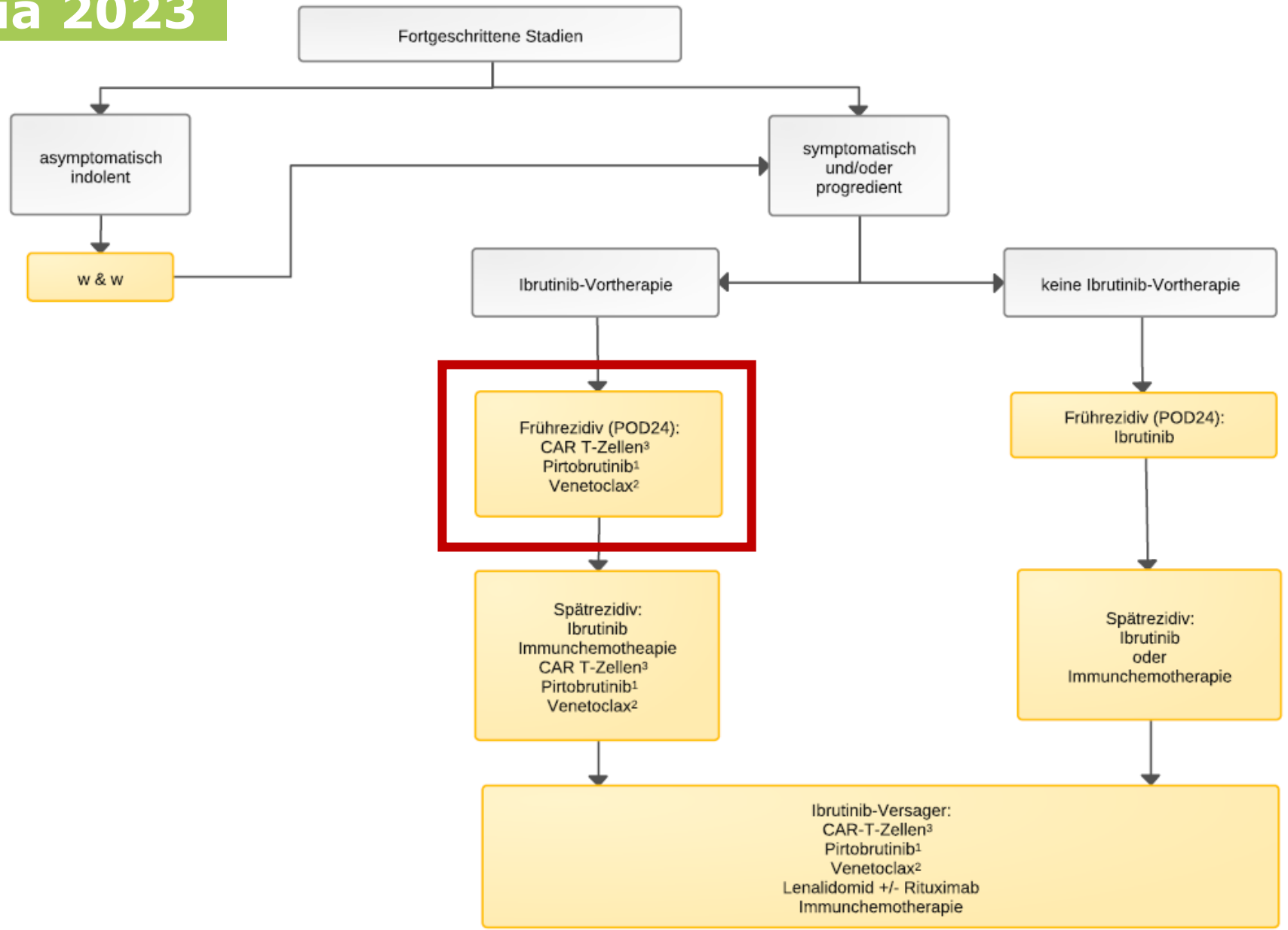
Relapsed Mantle cell Lymphoma

Onkopedia 2023



Relapsed Mantle cell Lymphoma

Onkopedia 2023



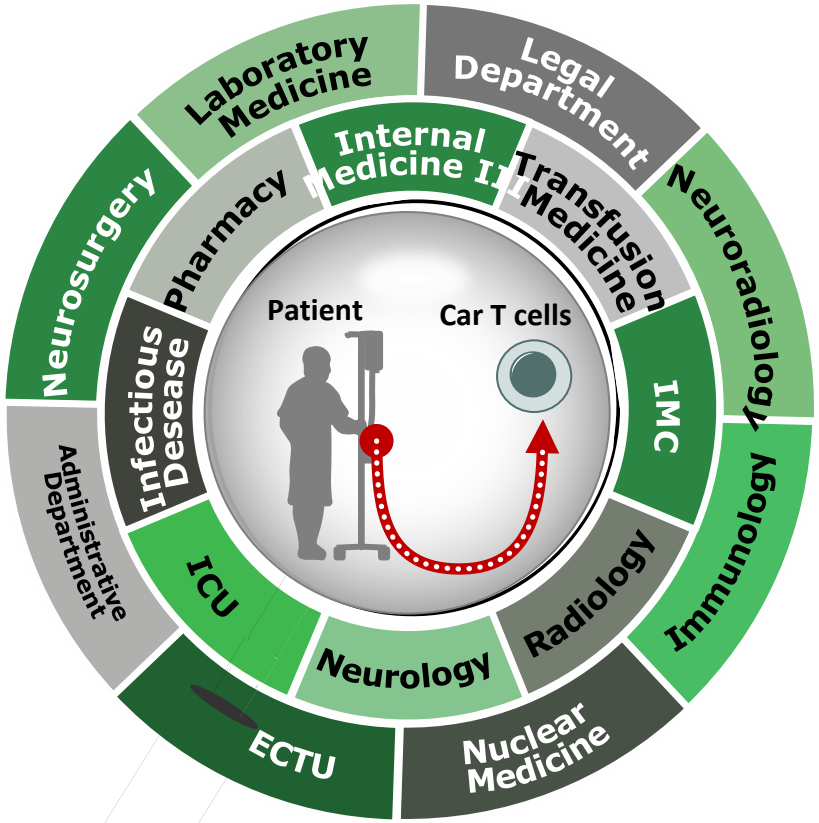
Interdisciplinary CAR-T Taskforce LMU Immunotherapy in Lymphoma

Building on a MEDIII Immuno-Taskforce based on T cell bispecifics Experience

IMP

- IMMune effector cells as Potent Actors of Cancer Therapy

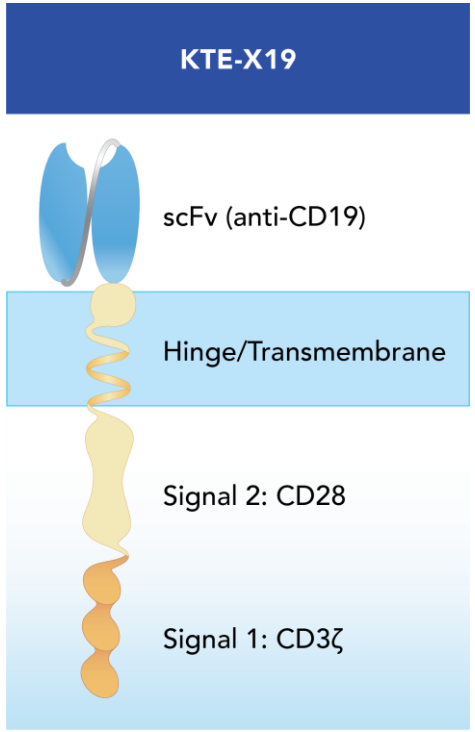
A Smartphone Application for the Mangement of CAR T and BiTE associated Toxicites



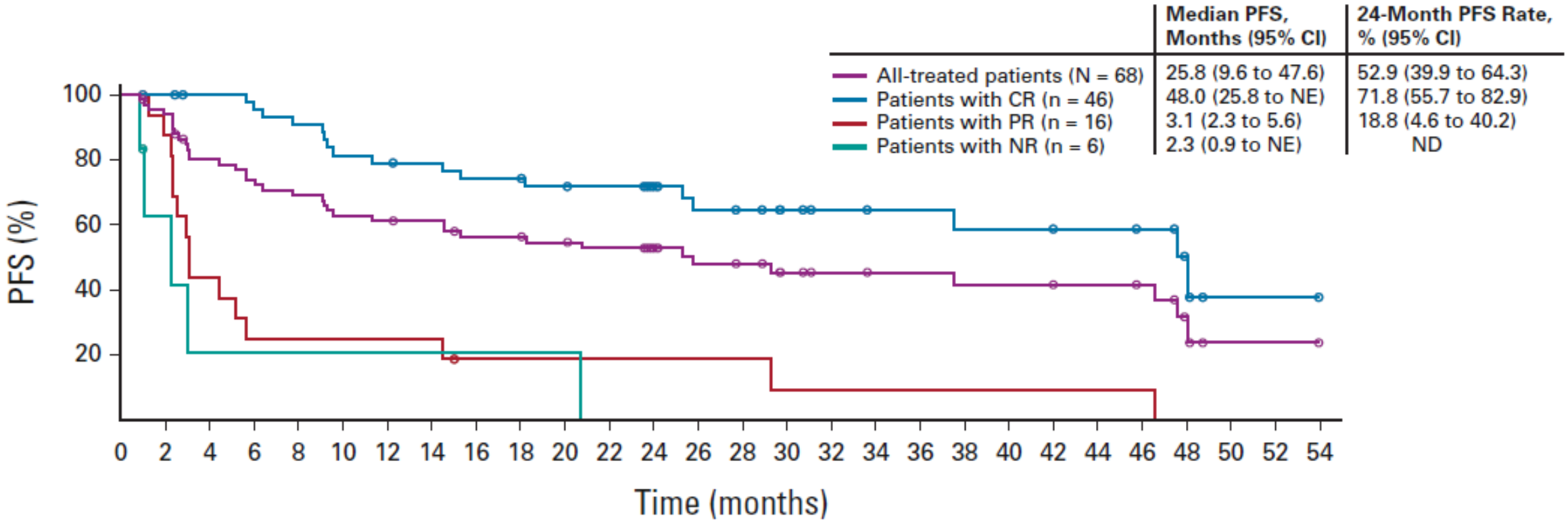
24/7: +49 89 2351 3208
CART@med.uni-muenchen.de

CAR-T cells in mantle cell lymphoma
Zuma 2: BTK failures

- Patients with R/R MCL have very poor outcomes
  - In patients who progress after BTK inhibitor therapy, ORR is 25% – 42% and OS is 6 – 10 months,[1-3] and few patients proceed to alloSCT
- KTE-X19 is a new anti-CD19 CAR T cell therapy containing a CD3ζ T cell activation domain and CD28 signaling domain
  - Manufacturing process removes circulating tumor cells[4]
- ZUMA-2 is a Phase 2, pivotal, multicenter, international study evaluating KTE-X19 in patients with R/R MCL



Relapsed Mantle cell Lymphoma (after BTKi)
CAR T-cells: Survival rates



No. at risk:

All-treated patients	68	62	51	47	44	40	39	38	34	34	32	30	24	20	19	15	13	12	12	11	11	10	10	9	4	1	1	0
Patients with CR	46	45	43	42	39	35	34	33	31	31	29	28	22	18	17	14	12	11	11	10	10	9	9	8	4	1	1	0
Patients with PR	16	14	7	4	4	4	4	4	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	0	0	0	0
Patients with NR	6	3	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

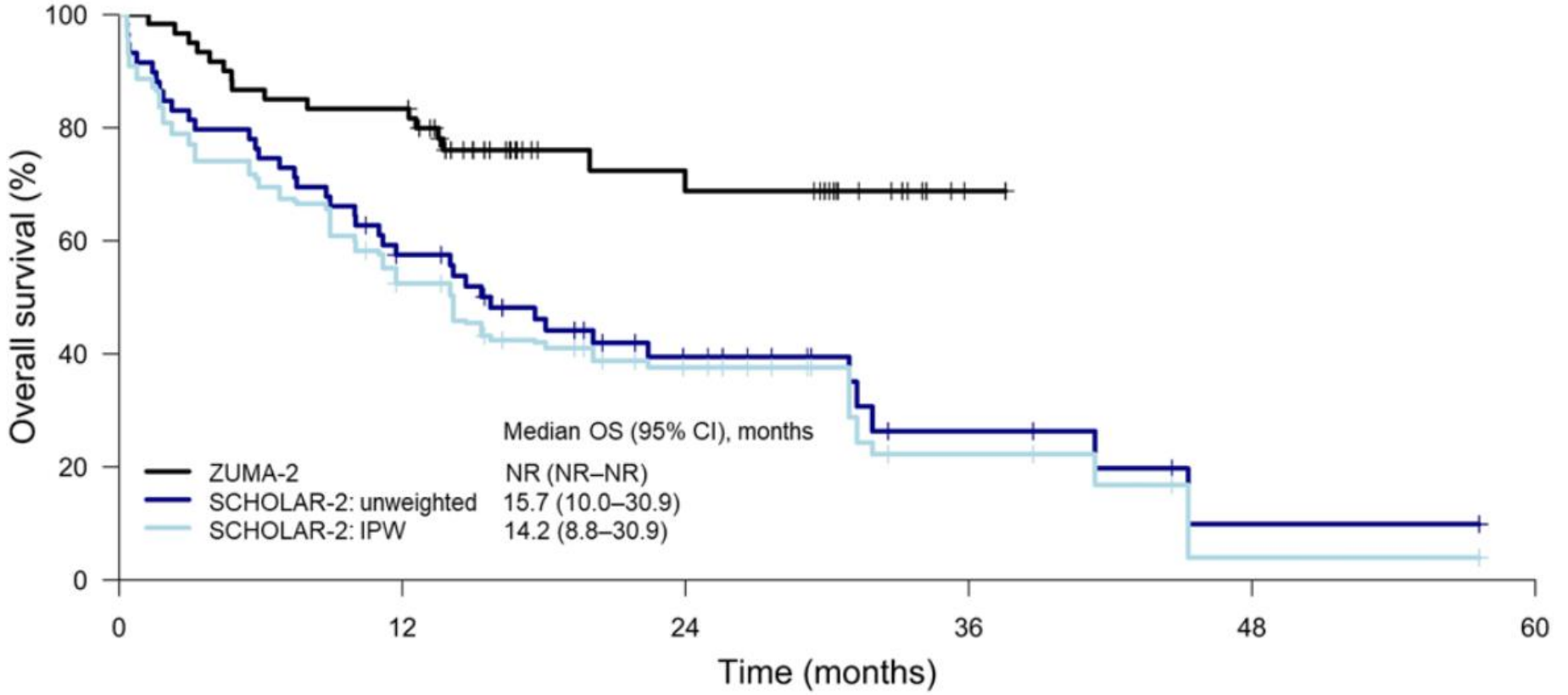
Wang, JCO 2022

KTE-X19 versus Standard of Care for Relapsed/Refractory Mantle Cell Lymphoma Previously Treated with Bruton Tyrosine Kinase Inhibitors: Real-World Evidence from Europe

EHA-1751

Georg Hess* [1], Martin Dreyling[2], Lucie Oberic[3], Eva Gine[4], Pier Luigi Zinzani[5], Kim Linton[6], Adam Vilmar[7], Mats Jerkeman [8], Jenny MH Chen[9], Anke Ohler[1], Stephan Stilgenbauer [10], Catherine Thieblemont[11], Jonathan Lambert[12], Vittorio Ruggero Zilioli[13], Juan Manuel Sancho[14], Ana Jimenez Ubieto[15], Luca Fischer[2], Sam Keeping[9], Julie E Park[9], Gregory A. Maglinte[16], Liliosa Nyamutswa[16], Rubina Siddiqi[16], John Reitan[17], Sally Wade[18], Gilles Salles[19]

1 Department of Hematology, Oncology and Pneumology, Comprehensive Cancer Center, University Medical School of the Johannes Gutenberg-University, Mainz, 2 Medizinische Klinik III, LMU Klinikum, Munich, Germany; 3Service d'Hématologie, Toulouse, France, 4 GELTAMO, Hematology Department, Hospital Clinic of Barcelona, Barcelona, Spain, 5 Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy, 6 The Christie Hospital, Manchester, United Kingdom, 7 Odense University Hospital, Odense, Denmark, 8 Lund University, Lund, Sweden, 9 PRECISIONBeon, Vancouver, Canada, 10 Department of Internal Medicine III, Ulm University, Ulm, Germany, 11 APHP, Hôpital Saint-Louis, Hemato-oncologie; Université de Paris, Paris, France, 12University College London Hospitals NHS Foundation Trust, London, United Kingdom, 13 Division of Hematology, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy, 14 GELTAMO, Institut Català d'Oncologia; Hospital Germans Trias I Pujol, Badalona, 15 GELTAMO, Hospital Doce de Octubre, Madrid, Spain, 16 Kite Pharma, Santa Monica, 17 RIM Group, LLC, Crown Point, 18 Wade Outcomes Research & Consulting, Salt Lake City, United States, 19 Centre Hospitalier Lyon Sud, Lyon, France



Number at risk
(number censored)

ZUMA-2	60 (0)	50 (0)	19 (25)	1 (43)	0 (44)	0 (44)
SCHOLAR-2 (unweighted)	59 (0)	32 (2)	15 (10)	5 (17)	1 (19)	0 (20)
SCHOLAR-2 (IPW)	59 (0)	30 (1)	15 (8)	4 (16)	0 (18)	0 (19)

Hess, Dreyling, EHA 2021, Leukemia Lymphoma 2023

Glofitamab dosing schedules

Phase I dose escalation in R/R MCL

Glofitamab IV administration

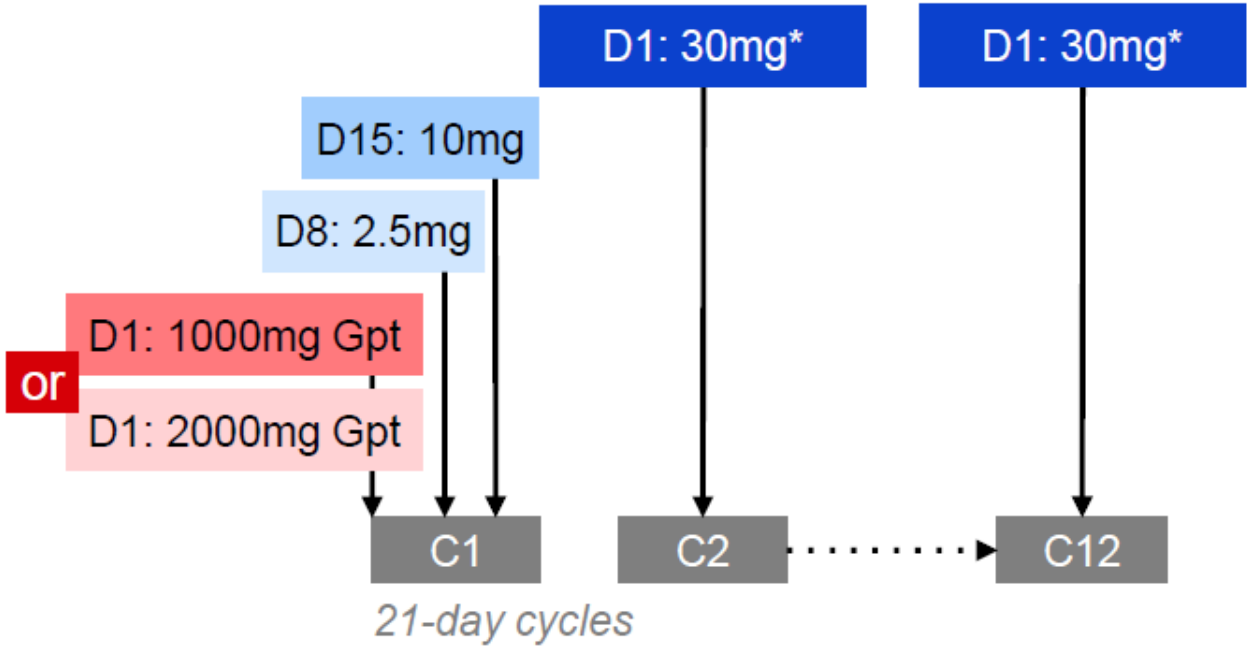
- Fixed-duration treatment: maximum 12 cycles

CRS mitigation

- Obinutuzumab pretreatment (1 x 1000mg or 1 x 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

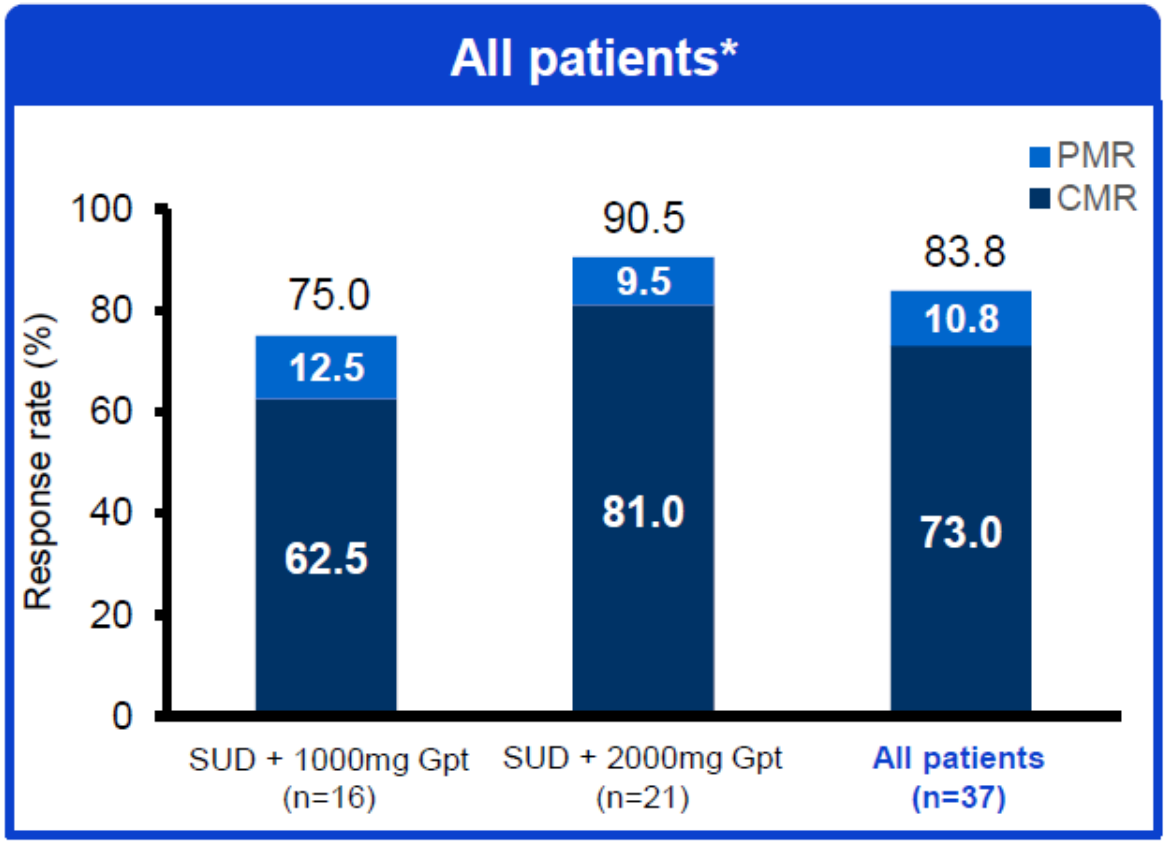
Population characteristics:

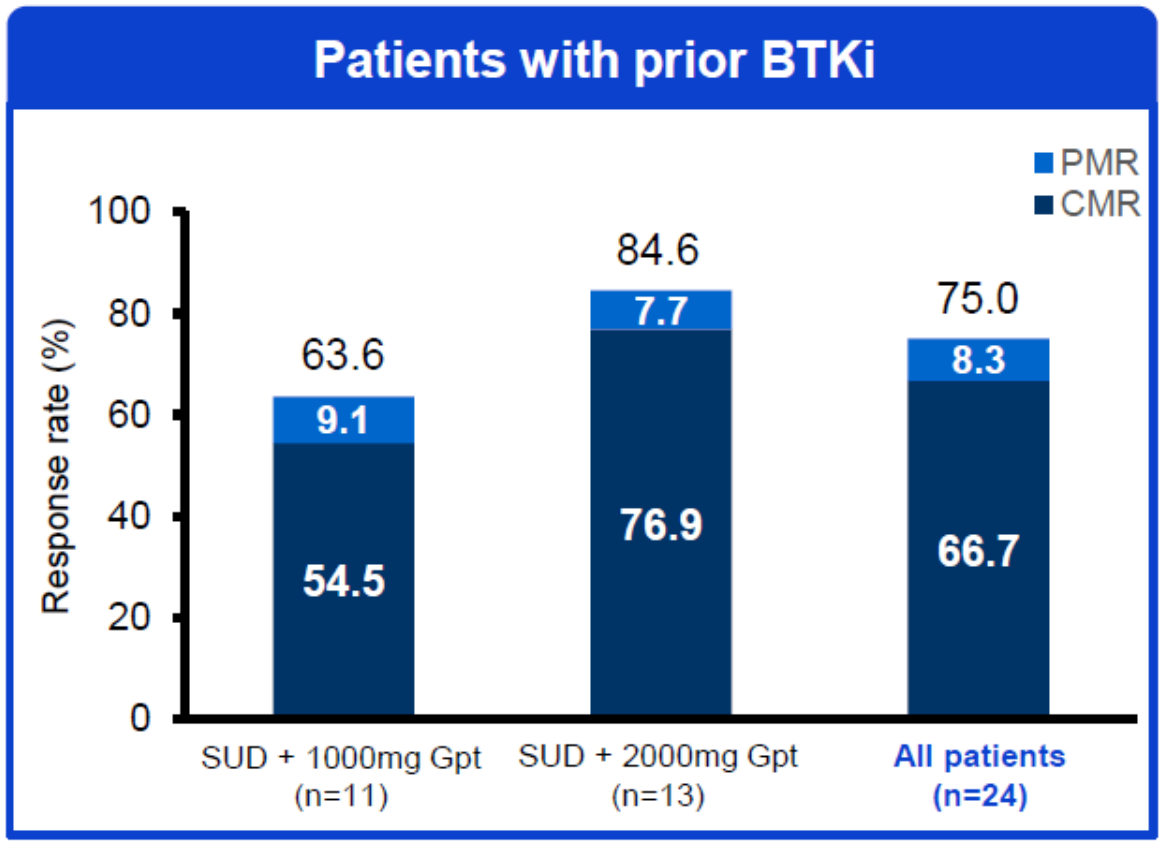
- Age ≥18 years
- ≥1 prior systemic therapy
- ECOG PS ≤1



Clinical cut-off date: March 14, 2022; *In the glofitamab SUD + 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose.

Response rates by glofitamab regimen





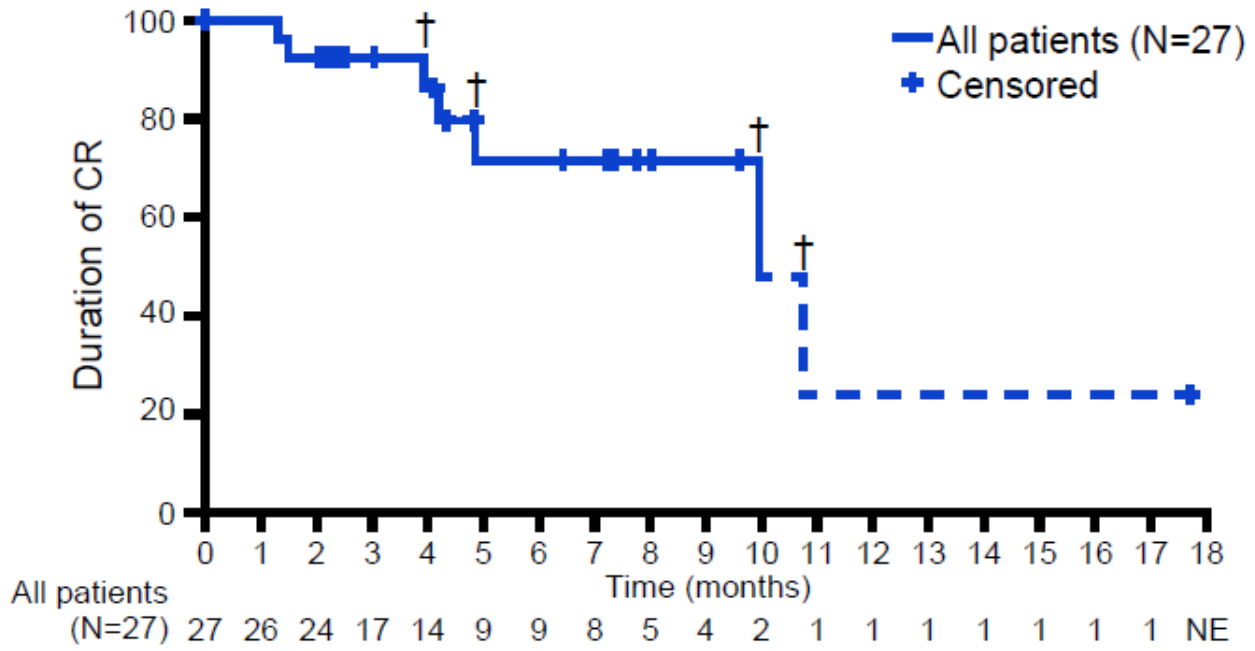
High response rates with glofitamab monotherapy in patients with R/R MCL

*Efficacy results are reported for the secondary efficacy population (includes all patients who had a response assessment performed, withdrew early from treatment or study, or are on still on treatment at the time of their first scheduled response assessment). Prior lines of therapy ranged from 1–5 in both the responder and non-responder groups. CMR, complete metabolic response; PMR, partial metabolic response.

Cheson et al. J Clin Oncol 2014.

Duration of complete response

Duration of CR*



- Median DOCR follow-up: 5.1 months (range, 0.0–18.0)
- Median DOCR: 10.0 months (95% CI: 4.9–NE)
- At data cut-off, **74.1%** (20/27) of patients with a CR remained in remission
- Durable CRs were maintained after cessation of therapy
- Four events due to COVID-19 deaths; when excluded, median not reached and 87% (20/23) CRs were ongoing

The majority of CRs were ongoing at data cut-off

*DOCR is measured from the date of first complete response to the date of progression or death from any cause; †Death due to COVID.
DOCR, duration of complete response.

Pirtobrutinib Safety Profile

	All Doses and Patients (N=725)			
	Treatment-Emergent AEs, (≥15%), %		Treatment-Related AEs, %	
Adverse Event (AEs)	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Fatigue	26.3%	1.7%	9.1%	0.8%
Diarrhea	22.1%	0.8%	8.6%	0.3%
Neutropenia[a]	21.7%	18.6%	13.0%	10.5%
Contusion	19.0%	0.0%	12.6%	0.0%
AEs of Special Interest[b]	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Bruising[c]	23.2%	0.0%	14.9%	0.0%
Rash[d]	12.3%	0.4%	5.5%	0.3%
Arthralgia	13.0%	0.4%	3.2%	0.0%
Hemorrhage/Hematoma[e]	10.2%	1.7%	3.4%	0.4%
Hypertension	9.5%	2.8%	3.2%	0.6%
Atrial fibrillation/flutter[f, g]	2.6%	1.0%	0.7%	0.1%

Median time on treatment for the overall population was 8 months

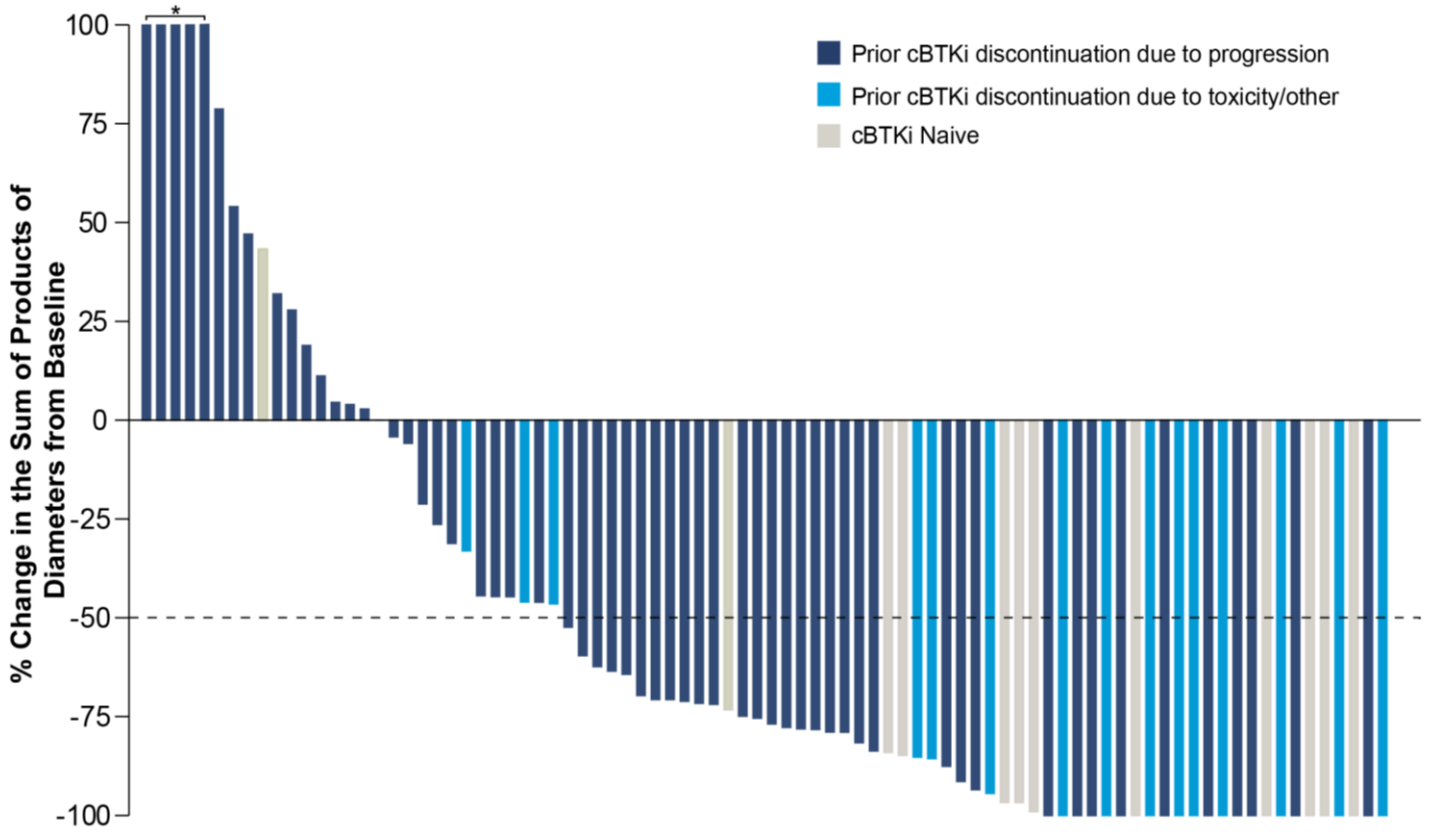
Discontinuations due to TRAEs occurred in 2% (n=15) of overall patients

Dose reductions due to TRAEs occurred in 5% (n=38) of overall patients

Overall and MCL safety profiles were consistent[h]

Data cutoff date of 31 January 2022. [a]Aggregate of neutropenia and neutrophil count decreased. [b]AEs of special interest are those that were previously associated with cBTKi. [c]Aggregate of contusion, petechiae, ecchymosis, and increased tendency to bruise. [d]Aggregate of all preferred terms including rash. [e]Aggregate of all preferred terms including hematoma or hemorrhage. [f]Aggregate of atrial fibrillation and atrial flutter. [g]Of 19 total afib/aflutter TEAEs, 6 occurred in patients with a prior medical history of atrial fibrillation. [h]MCL safety population data can be found via QR code.

Pirtobrutinib Efficacy in Patients with MCL



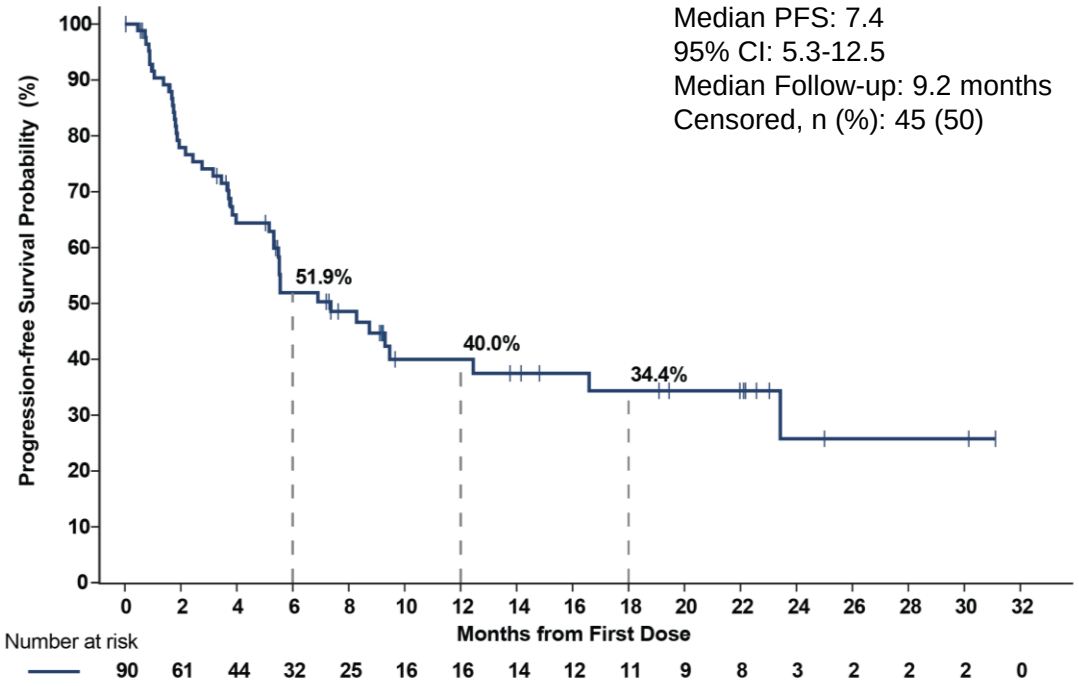
Prior cBTKi MCL Patients	n=90
Overall Response Rate[a], % (95% CI)	**57.8% (46.9-68.1)**
Best Response[b]	
CR, n (%)	18 (20.0)
PR, n (%)	34 (37.8)
SD, n (%)	14 (15.6)
PD, n (%)	15 (16.7)

cBTKi Naïve MCL Patients	n=14
Overall Response Rate[a], % (95% CI)	**85.7% (57.2-98.2)**
Best Response[c]	
CR, n (%)	5 (35.7)
PR, n (%)	7 (50.0)
SD, n (%)	0 (0.0)
PD, n (%)	1 (7.1)

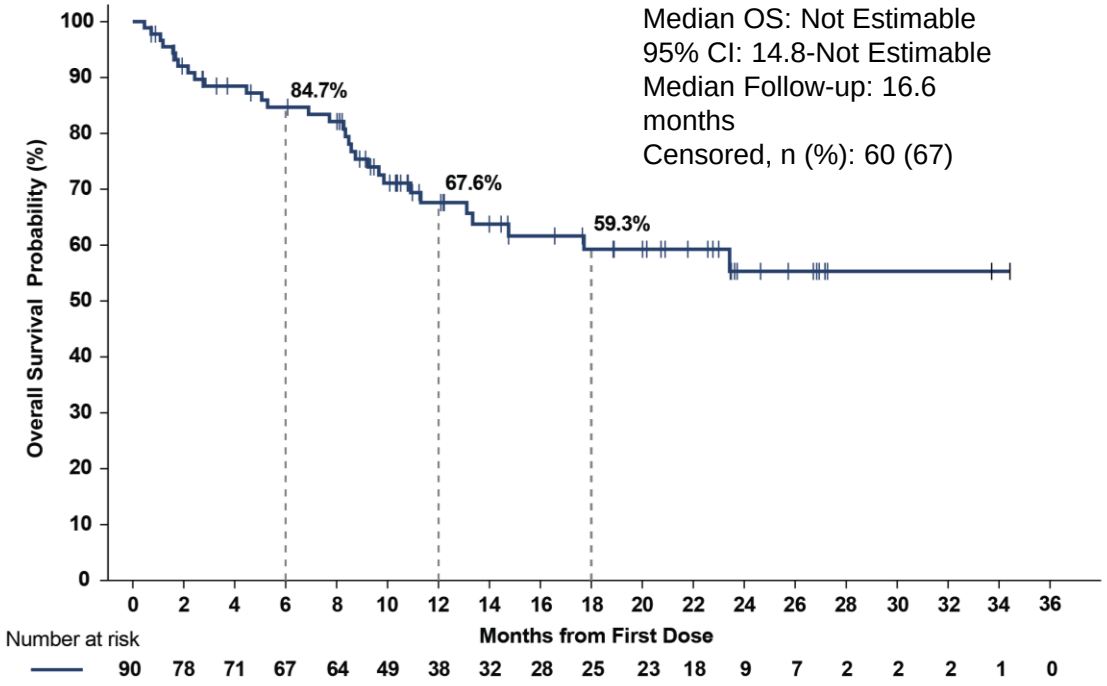
Data cutoff date of 31 January 2022. Data for 18 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. [a]ORR includes patients with a best response of CR and PR. [b]9 cBTKi pre-treated MCL patients were not evaluable. [c]1 cBTKi naïve patient was not evaluable. Response status per Lugano 2014 criteria based on IRC assessment.

Pirtobrutinib Progression-Free Survival and Overall Survival in Prior cBTKi MCL

Progression-Free Survival

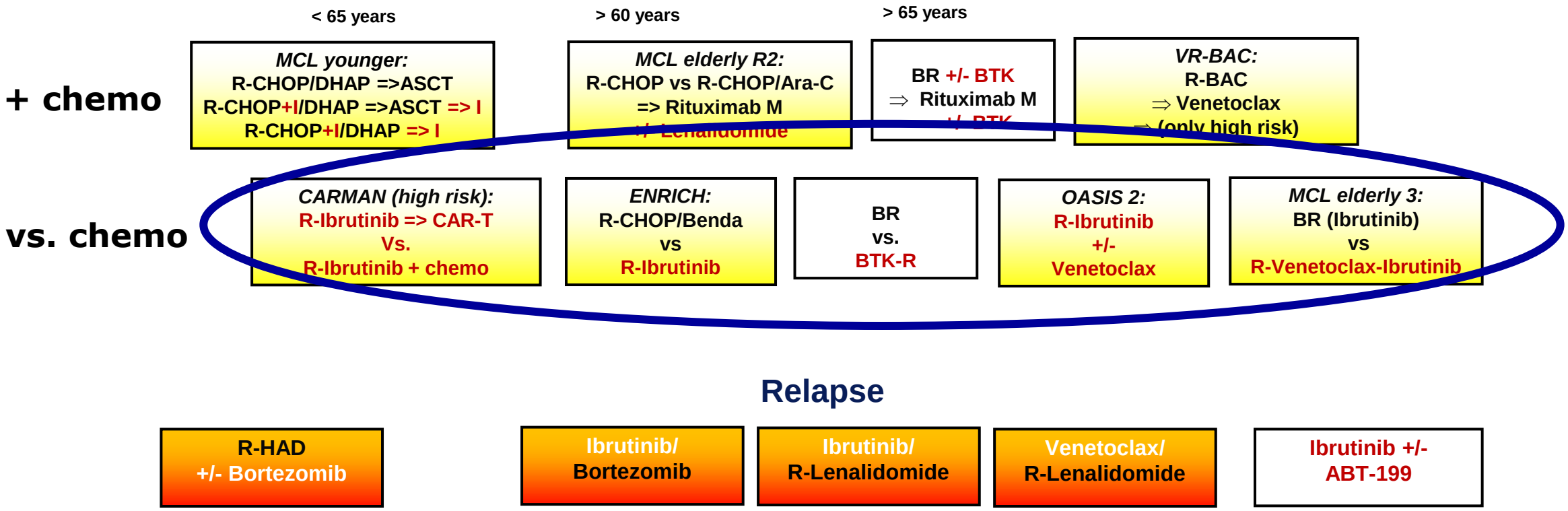


Overall Survival



Data cutoff date of 31 January 2022. Response status per Lugano 2014 criteria based on IRC assessment.

European MCL Network
Study generation 2023



Relapse

R-HAD +/- Bortezomib	Ibrutinib/ Bortezomib	Ibrutinib/ R-Lenalidomide	Venetoclax/ R-Lenalidomide	Ibrutinib +/- ABT-199

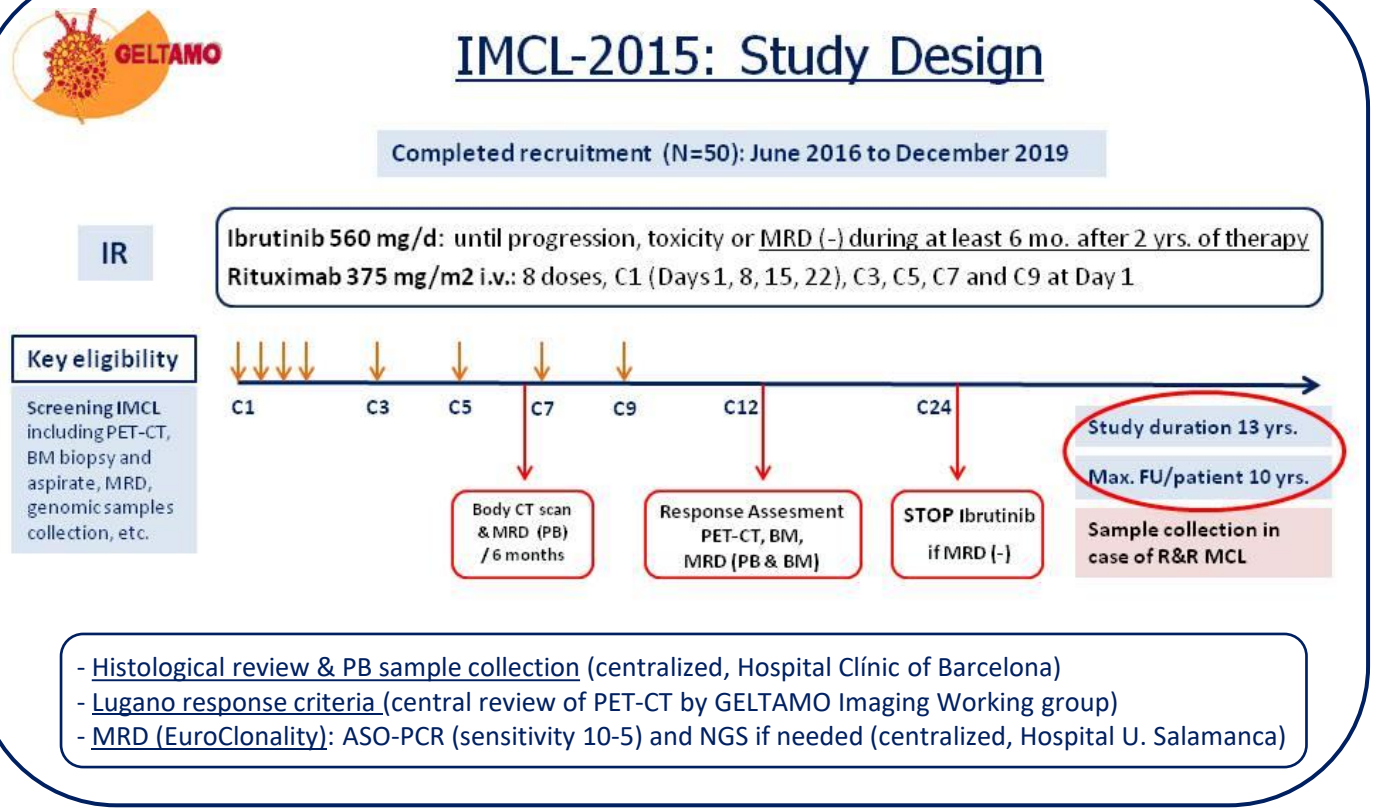
IMCL-2015

"Multicentric phase II trial to evaluate the efficacy and safety of Ibrutinib in combination with rituximab in patients with indolent clinical forms of Mantle Cell Lymphoma"

Phase II (N= 50 patients, 14 GELTAMO sites)

- Upfront Ibrutinib + Rituximab combination in IMCL
- Biological studies: IGHV mutational study, DNA copy number, *WGS/WES* and epigenetic studies in PB samples (and tissue when possible) before treatment and in case of relapse

IMCL-2015: Study Design



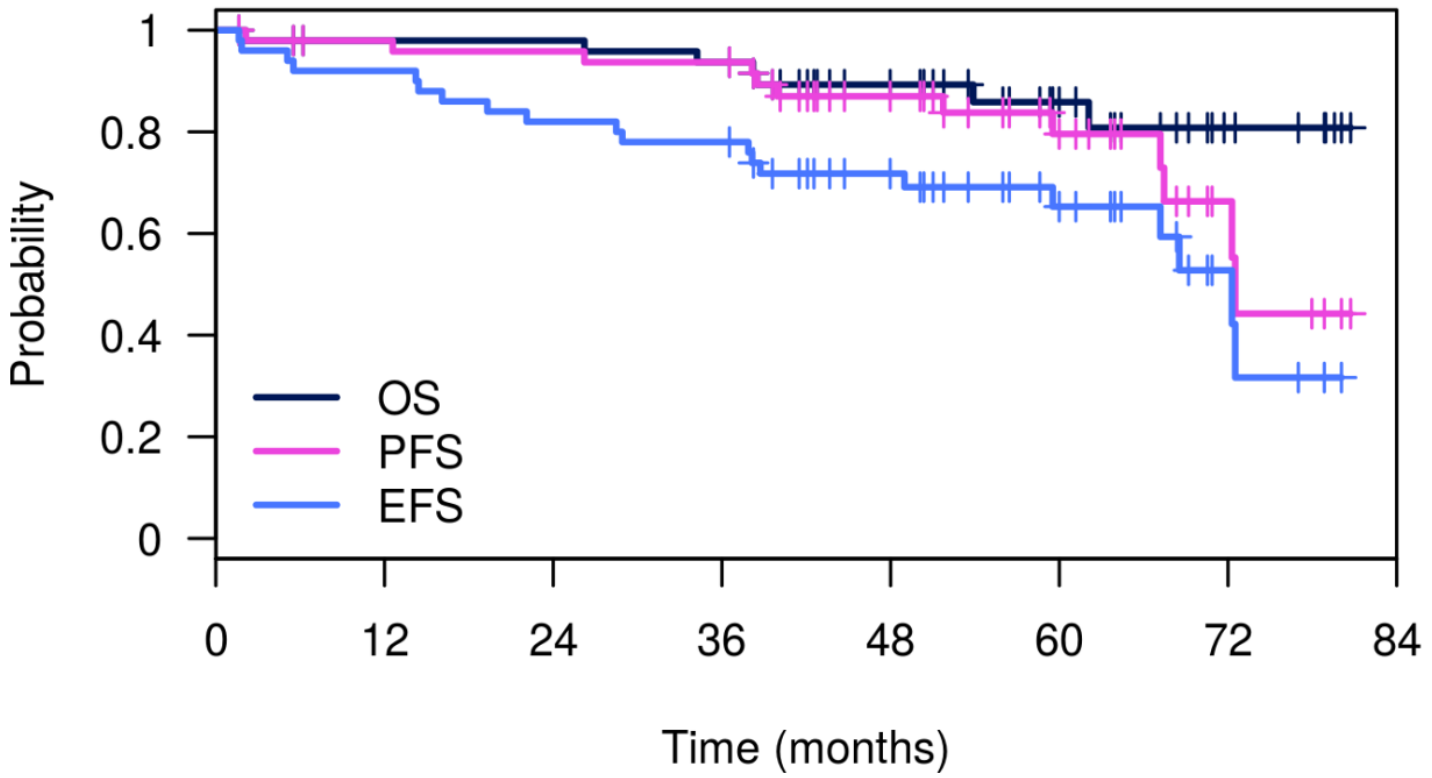
Key inclusion and exclusion criteria:

- Asymptomatic MCL patients, no prior treatments, observation for at least 3 months
- Eligible both leukemic non nodal presentations and cases with lymph nodes < 3 cm and Ki67 < 30%
- Blastoid variants excluded

Gine, ICML 2023

E Giné et al, JCO 2022;40(11):1196-1205

IMCL-2015: SURVIVAL



No. at risk:

OS	50	46	46	44	31	19	7	0
PFS	50	46	45	44	30	18	6	0
EFS	50	46	41	39	27	16	5	0

5-yr OS: 86% (CI95%: 75-97)

5-yr PFS: 80% (CI95%: 66-93)

5-yr EFS: 65% (CI95%: 50-79)

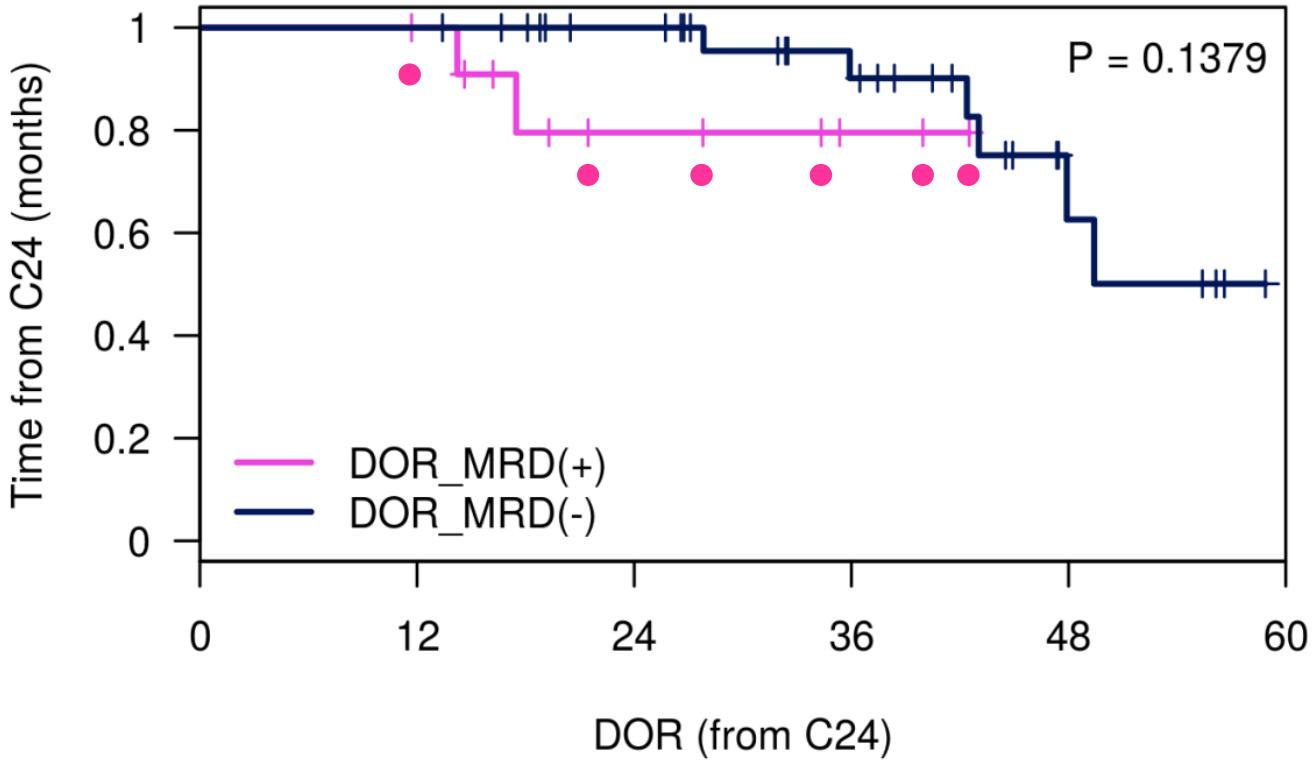
Median PFS: 72 months (CI 95%: 66-79)

(Data cut-off 15 March 2023)

Gine, ICML 2023

IMCL-2015: DOR from C24 According to MRD Status and Ibrutinib Discontinuation

DOR from C24 evaluation (n=44)



No. at risk:

DOR_MRD(+)	12	11	5	2	0	0
DOR_MRD(-)	32	32	26	17	5	0

- **MRD (-) / Ibrutinib discontinuation (n=32)**
  - **Progression (n=6)**
- **MRD (+) / Ibrutinib ongoing (n=12)**
  - **Progression (n=2)**

- MRD (-): 20 /32 (63%) patients continue MRD (-) at last control

- MRD(+): 6/12 (50%) patients continue on Ibrutinib

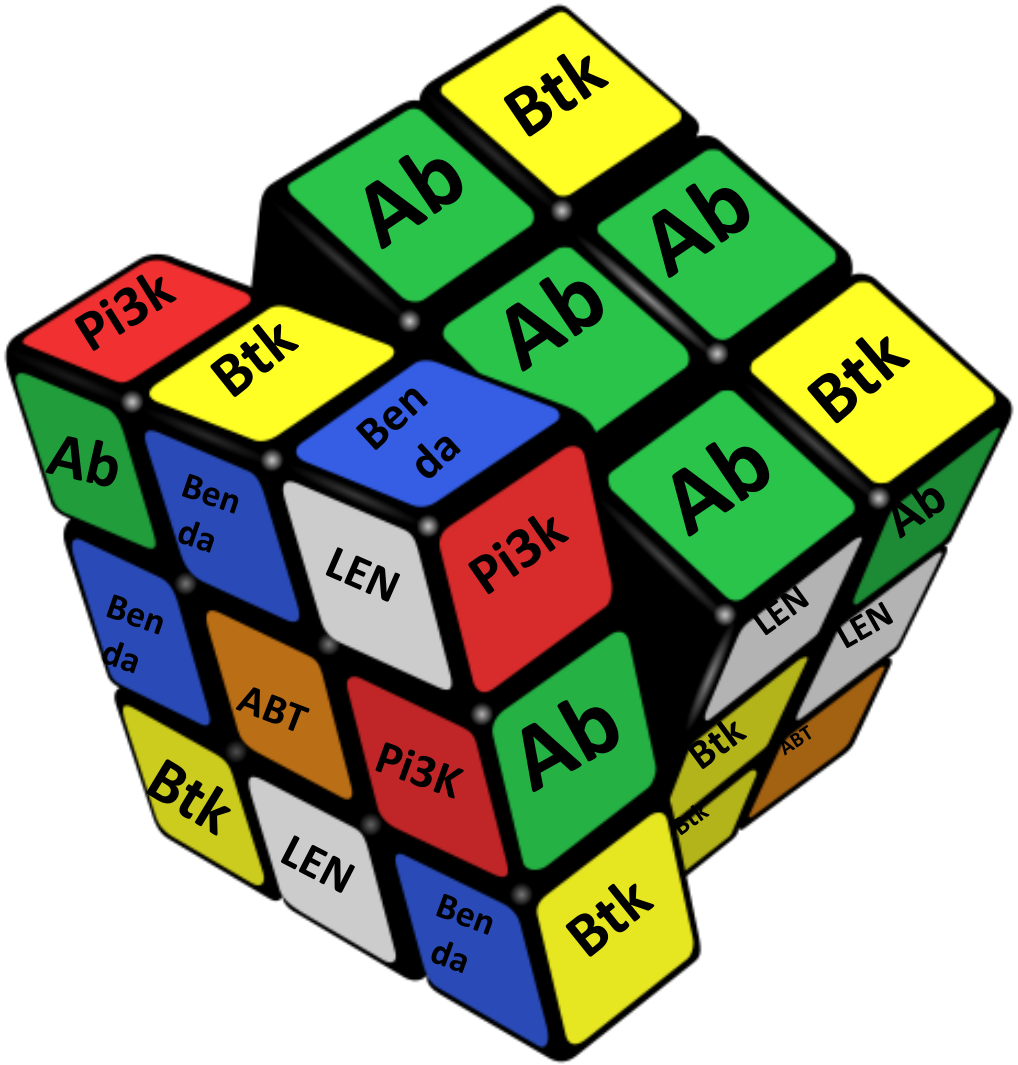
● Ibrutinib ongoing

Medians DOR: not reached

Gine, ICML 2023

(Data cut-off 20 March 2023)

Mantle cell lymphoma
The era of combinations

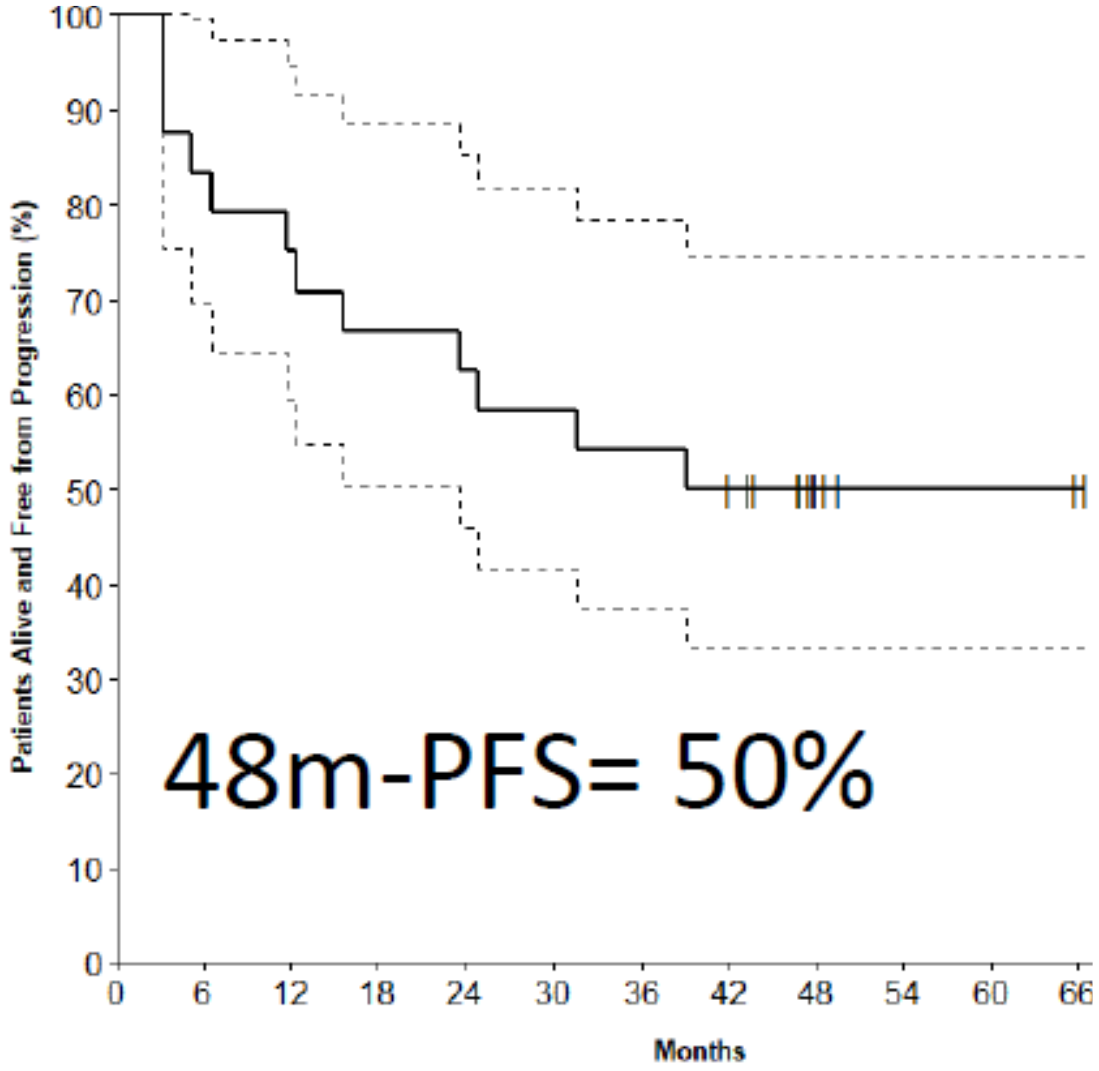


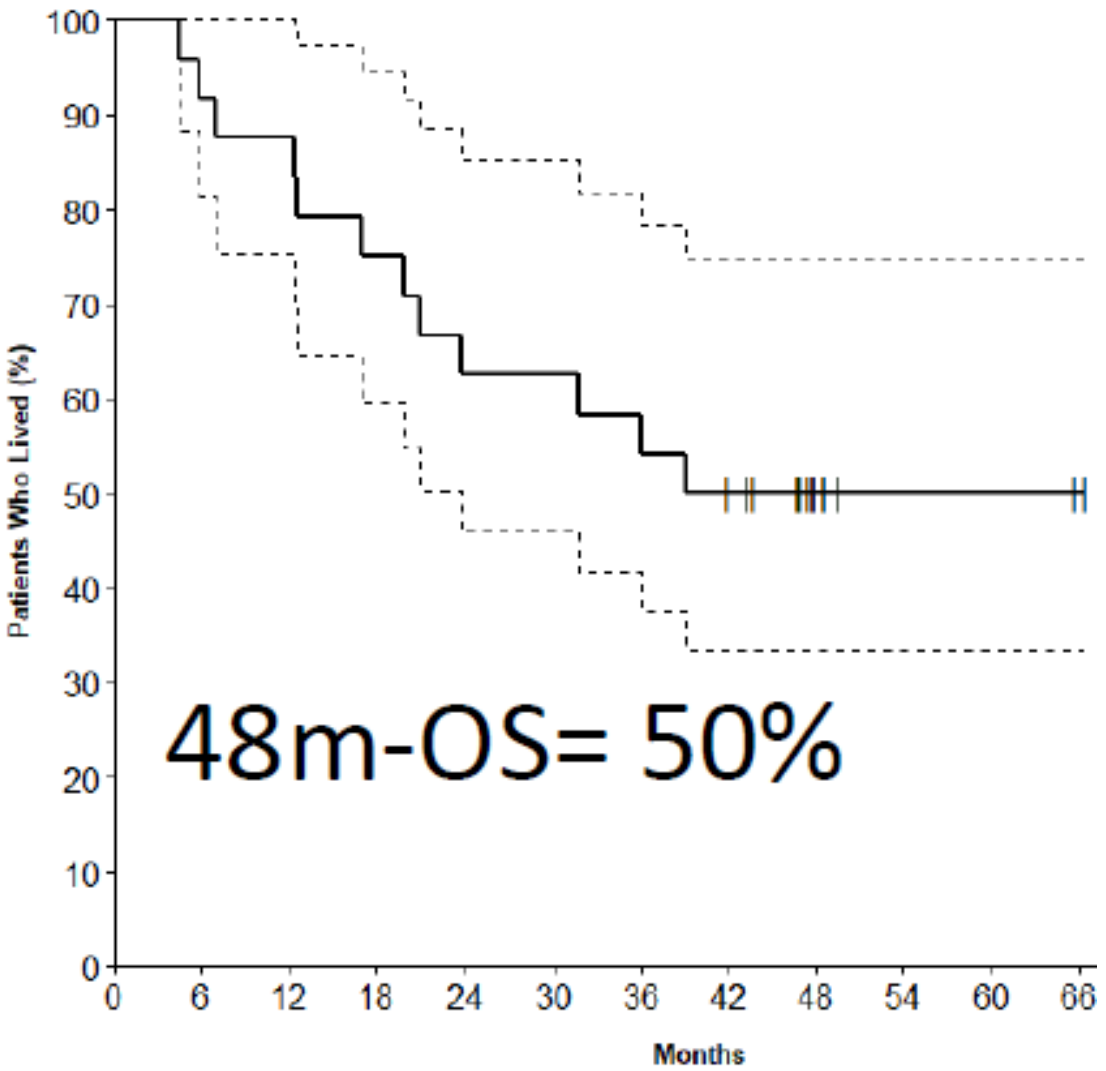
OASIS: TREATMENT SCHEDULE

	Cycle 1				Cycle 1 bis				Cycle 2				cycles	Maintenance	
Baseline	**W1**	**W2**	**W3**	**W4**	**W1**	**W2**	**W3**	**W4**	**W1**	**W2**	**W3**	**W4**	**C3-C6**	**C7-C23**	**until prog**
Ibrutinib (560mg/d)	**D2**	→	→	→	→	→	→	→	→	→	→	→	→	→	→
Obinutuzumab (1g)	**D1**	**D8**	**D15**		**D1**				**D1**				**D1 each cycle**	**D1 every 2 cycles from C8**	
Venetoclax (mg/d)					**20**	**50**	**100**	**200**	**400**	**400**	**400**	**400**	→	→	

Le Gouill, EHA 2020; Blood 2021

Relapsed Mantle cell lymphoma
OASIS long term follow-up



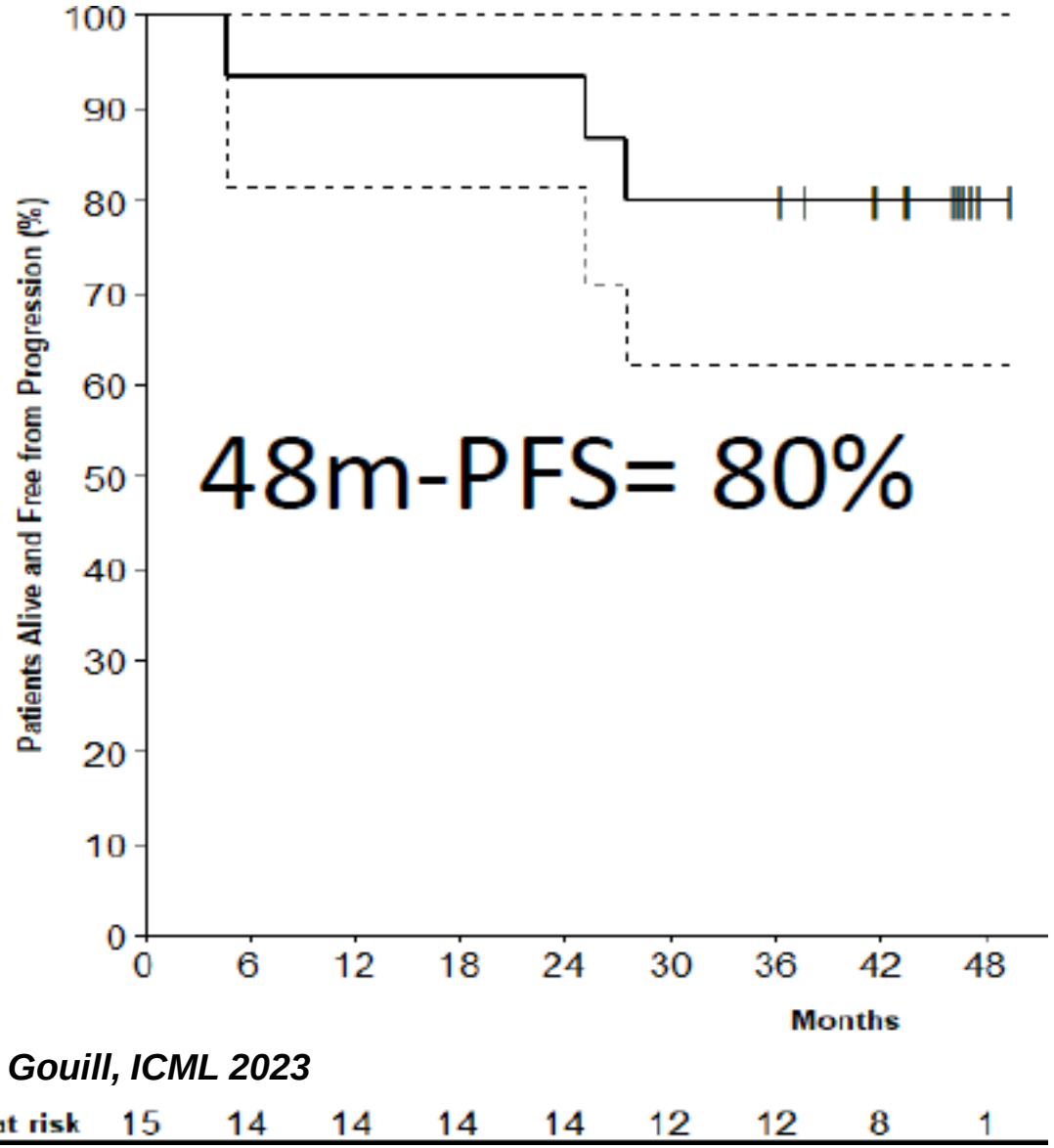


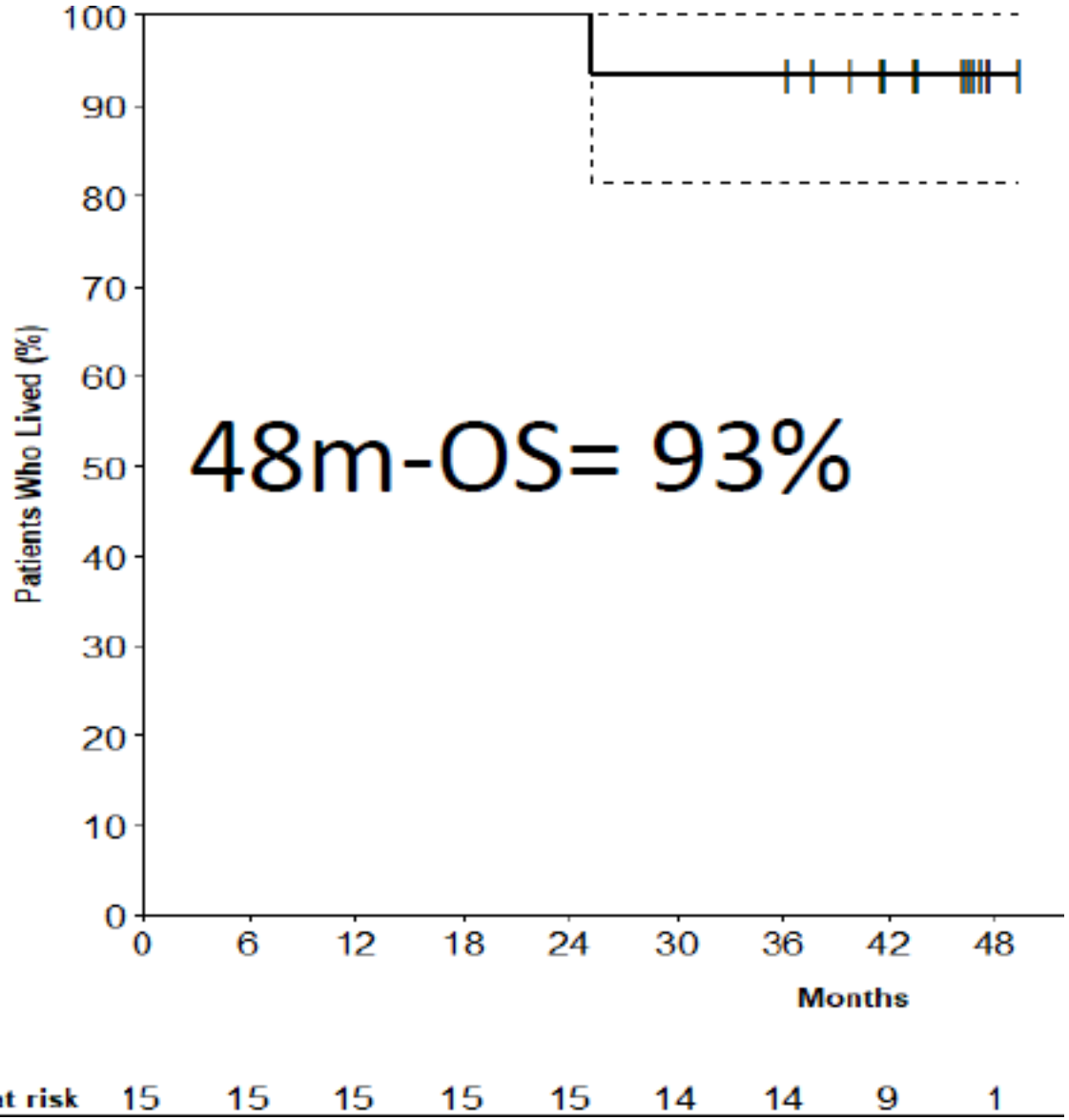
Le Gouill, ICML 2023

No. at risk	24	20	18	16	15	14	13	11	4	2	2	1

No. at risk	24	22	21	18	15	15	14	11	4	2	2	1

First line Mantle cell lymphoma
OASIS long term follow-up

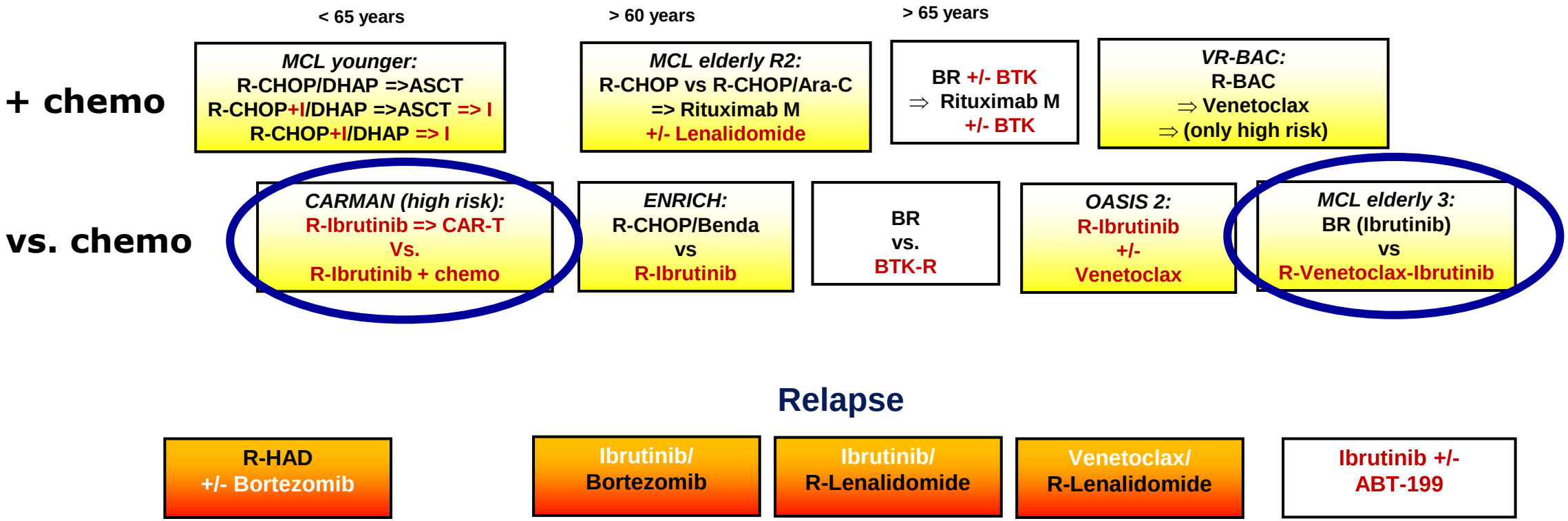




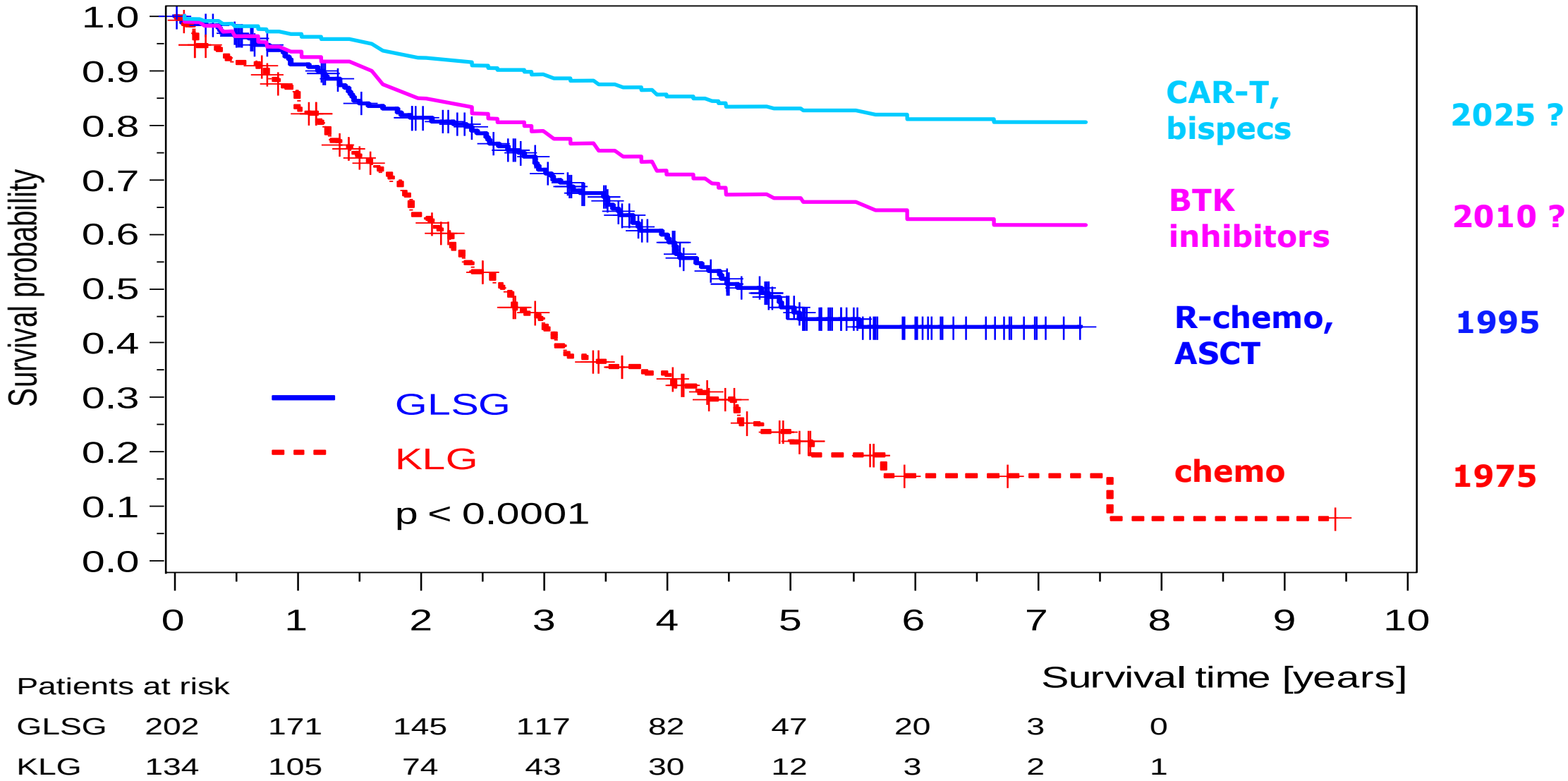
Le Gouill, ICML 2023

European MCL Network
Study generation 2023

LMU KLINIKUM



MCL: Auf dem Weg zur Heilung ?



Herrmann JCO 2009

TRIANGLE: 23rd annual meeting in Sevilla 2022