3rd edition

Unmet challenges in high risk hematological malignancies: from benchside to clinical practice

Turin, September 21-22, 2023

Starhotels Majestic

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Disclosures of Georg Hess

–**Consultancy**: Abbvie, ADC-Therapeutics, AstraZenaeca, BMS, Genmab, Gilead/Kite, Incyte, Janssen, Lilly, Miltenyi, Novartis, Roche

–**Honoraria**: Abbvie, AstraZeneca, Beigene, BMS, Genmab, Gilead/Kite, Incyte, Janssen, Lilly, Roche

–**Research Funding**: Abbvie, Gilead/Kite, Incyte, Janssen, Morphosys, Roche

–**Patents and Royalties**: not applicable

–**Membership on an entity's Board of Directors or advisory committees**: not applicable

–**Discussion of off-label drug use**: not applicable

–**Travel grants**: Gilead/Kite, Janssen

Mantle cell lymphoma – First line treatment – focus on High Risk

Georg Heß | Department of Hematology and Medical Oncology|
University Medical School of the Johannes Gutenberg-University, Mainz, Germany

A Clinical Analysis of Two Indolent Lymphoma Entities: Mantle Cell Lymphoma and Marginal Zone Lymphoma (Including the Mucosa-Associated Lymphoid Tissue and Monocytoid B-Cell Subcategories): A Southwest Oncology Group Study

By Richard I. Fisher, Steve Dahlberg, Bharat N. Nathwani, Peter M. Banks, Thomas P. Miller, and Thomas M. Grogan

Blood, Vol 85, No 4 (February 15), 1995: pp 1075-1082

In summary, patients with advanced stage MZL have a clinical course similar to that of other patients in WF A through E, although patients with advanced stage MALT lymphomas may have a more aggressive course than previously recognized. However, patients with MCL do not have an indolent lymphoma and are candidates for innovative therapy.

Efficacy of Four Different Regimens in 64 Mantle-Cell Lymphoma Cases: Clinicopathologic Comparison With 498 Other Non-Hodgkin's Lymphoma Subtypes

By I. Teodorovic, S. Pittaluga, J.C. Kluin-Nelemans, J.H. Meerwaldt, A. Hagenbeek, M. van Glabbeke, R. Somers, L. Bijnens, E.M. Noordijk, and C. De Wolf Peeters for the European Organization for the Research and Treatment of Cancer Lymphoma Cooperative Group

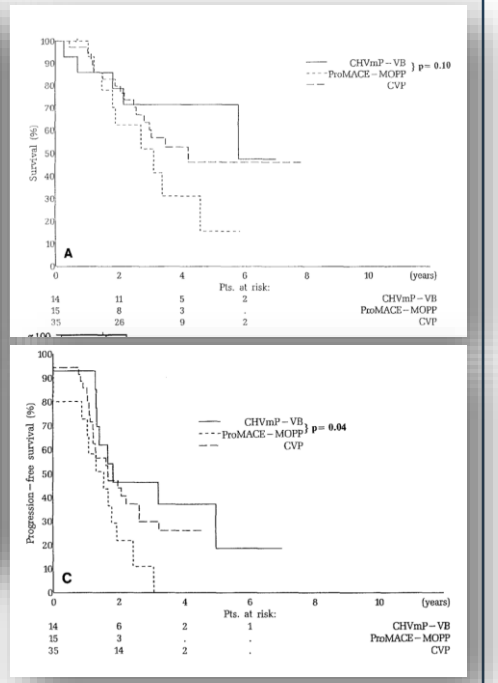
Purpose: **Before recognizing mantle-cell lymphoma (MCL) as a distinct entity, these patients were grouped into low-grade (LG) or intermediate-/high-grade categories (IGHG) according to the Working Formulation and received various therapies. This was a unique opportunity to evaluate characteristics, behavior, response to treatment, and outcome of patients with MCL from two phase III trials conducted by the European Organization for the Research and Treatment of Cancer (EORTC): EORTC 20855 IGHG and EORTC 20856 LG.**

Patients and Methods: **After histologic review, 64 diagnosed MCL patients (29 IGHG and 35 LG) were compared with other patients in their respective trials. In the IGHG group, patients received cyclophosphamide, doxorubicin, teniposide (VM_{26}), prednisone, vincristine, and bleomycin (CHVmP-VB) or modified doxorubicin, cyclophosphamide, etoposide (VP16), mechlorethamine, vincristine, procarbazine, and prednisone (ProMACE-MOPP). In the LG group, after receiving cyclophosphamide, vincristine, and prednisone (CVP) induction, patients were randomized between maintenance treatment with interferon alfa-2a (IFN) or no further treatment.**

Results: **MCL patients compared with IGHG subtypes showed a similar overall survival and response rate, but shorter duration of response and progression-free survival. Comparing with LG patients, their response rate, duration of response, and progression-free survival showed no difference, while their overall survival was nearly twice shorter. MCL patients treated with CHVmP-VB had the longest survival. No treatment showed any significant improvement in terms of progression-free survival.**

Conclusion: **These data confirm that MCL represents a clinicopathologic entity. In terms of survival, it behaves like IGHG subtypes, while in terms of progression-free survival, it behaves like LG lymphoma. It is still not clear which first-line treatment offers patients with MCL the best chance to obtain both a complete response (CR) and a long-term survival.**

J Clin Oncol 13:2819-2826. © 1995 by American Society of Clinical Oncology.



Mantle-Cell Lymphomas Have More Widespread Disease and a Slower Response to Chemotherapy Compared With Follicle-Center Lymphomas: Results of a Prospective Comparative Analysis of the German Low-Grade Lymphoma Study Group

By Wolfgang Hiddemann, Michael Unterhalt, Richard Herrmann, Hans-Heinrich Wöltjen, Ernst-Dietrich Kreuser, Lorenz Trümper, Monika Reuss-Borst, Elke Terhardt-Kasten, Mechthild Busch, Andreas Neubauer, Ulrich Kaiser, Rolf-Dieter Hanrath, Helmut Middeke, Gisela Helm, Mathias Freund, Harald Stein, Markus Tiemann, and Reza Parwaresch

Purpose: **To compare mantle-cell lymphomas (MCLs) and follicle-center lymphomas (FCLs) for their features of clinical presentation, response to chemotherapy, and prognosis on the basis of a prospective randomized clinical trial.**

Patients and Methods: **Patients with MCL and FCL who entered onto the prospective randomized comparison of cyclophosphamide, vincristine, and prednisone (COP) versus prednimustine and mitoxantrone (PmM) followed by a second randomization for interferon (IFN) maintenance versus observation only.**

Results: **One hundred sixty-five of 234 patients had FCL and 45 of 234 patients had MCL. With FCL, both sexes were equally affected (men, 47%); patients with MCL were predominantly men (78%; $P < .0004$) and had a higher median age (64 v 53 years; $P < .0001$). Patients with MCL also had more widespread disea- reflected by the proportion of patients with two greater extranodal manifestations (43% v 21%; P .005) and nine or greater involved nodal areas (64% 45%; nonsignificant [NS]). Response to chemotherapy was significantly lower in patients with MCL (complete remission [CR] + partial remission [PR], 69% v 88%; $P < .05$) and occurred at a slower pace. Patients with MCL also had a shorter event-free interval (median, 8 v 24 months; $P < .0001$) and overall survival (median, 28 v 77 months; $P < .0001$). In both subtypes, however, patients with less than two residual lymphoma manifestations in remission experienced a relatively good prognosis with an estimated 5-year survival of greater than 60% for MCL and greater than 75% for FCL.**

Conclusion: **MCL and FCL differ substantially in their features of presentation, response to chemotherapy, and long-term prognosis. The extent of residual disease after completion of chemotherapy discriminates patients with different prognosis and may be used for the**

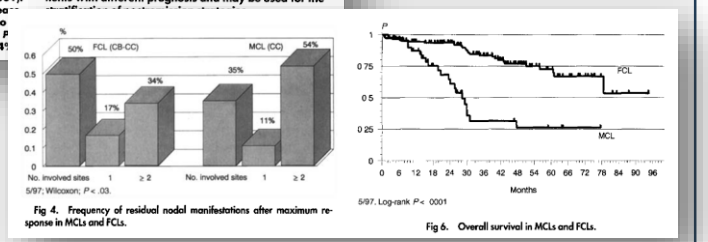


Fig 4. Frequency of residual nodal manifestations after maximum response in MCLs and FCLs.

Fig 6. Overall survival in MCLs and FCLs.

Development steps of treatment of MCL

- Establishment of
  - Dose intensification (HDT)
  - Introduction of especially active cytostatics (cytarabinosid, bendamustine)
  - Identification of effective targeted agents (Proteasome inhibitors, BTKi, BCL-2i, Celmods)
  - Introduction of T-cell engaging therapies

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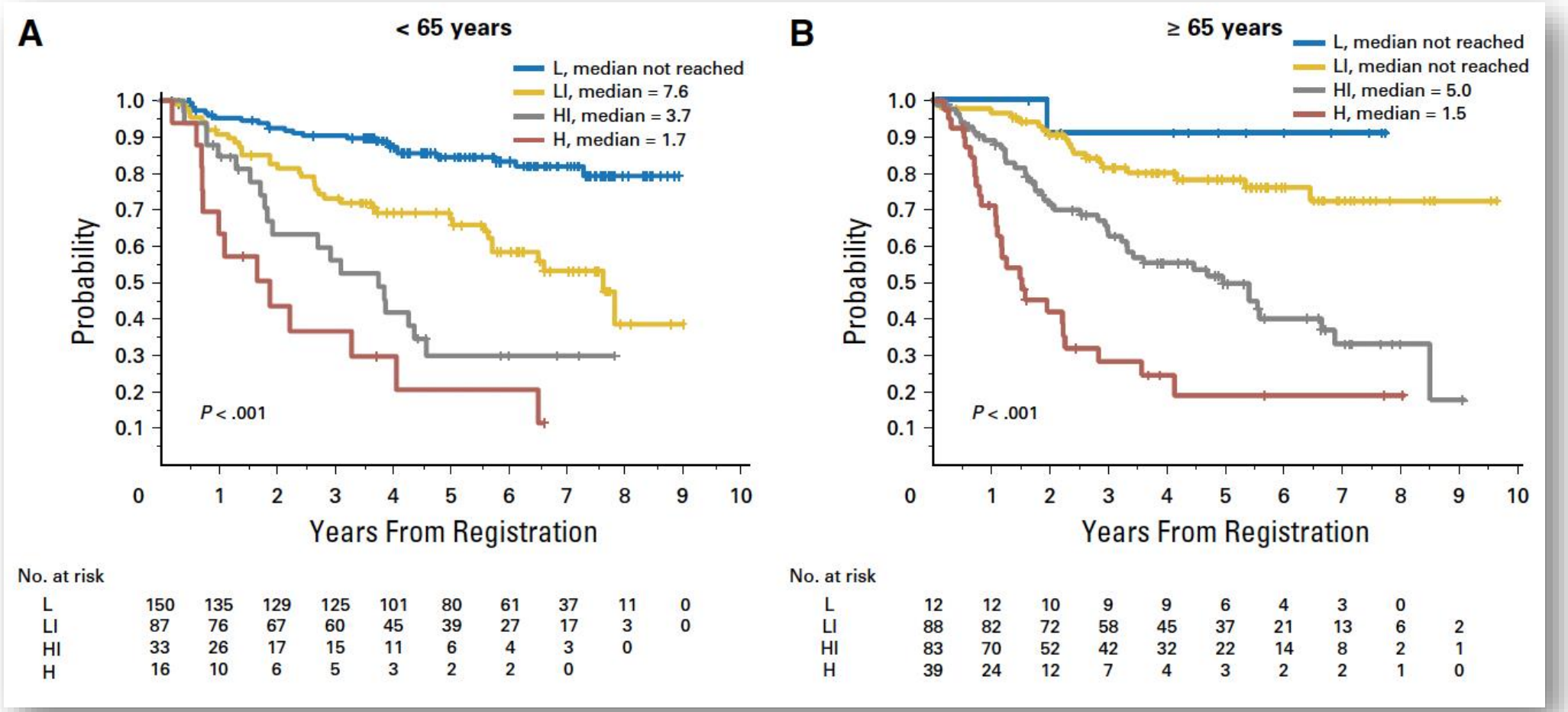
  - Identification of effective targeted agents (Proteasome inhibitors, BTKi, BCL-2i, Celmods)
  - Introduction of T-cell engaging therapies

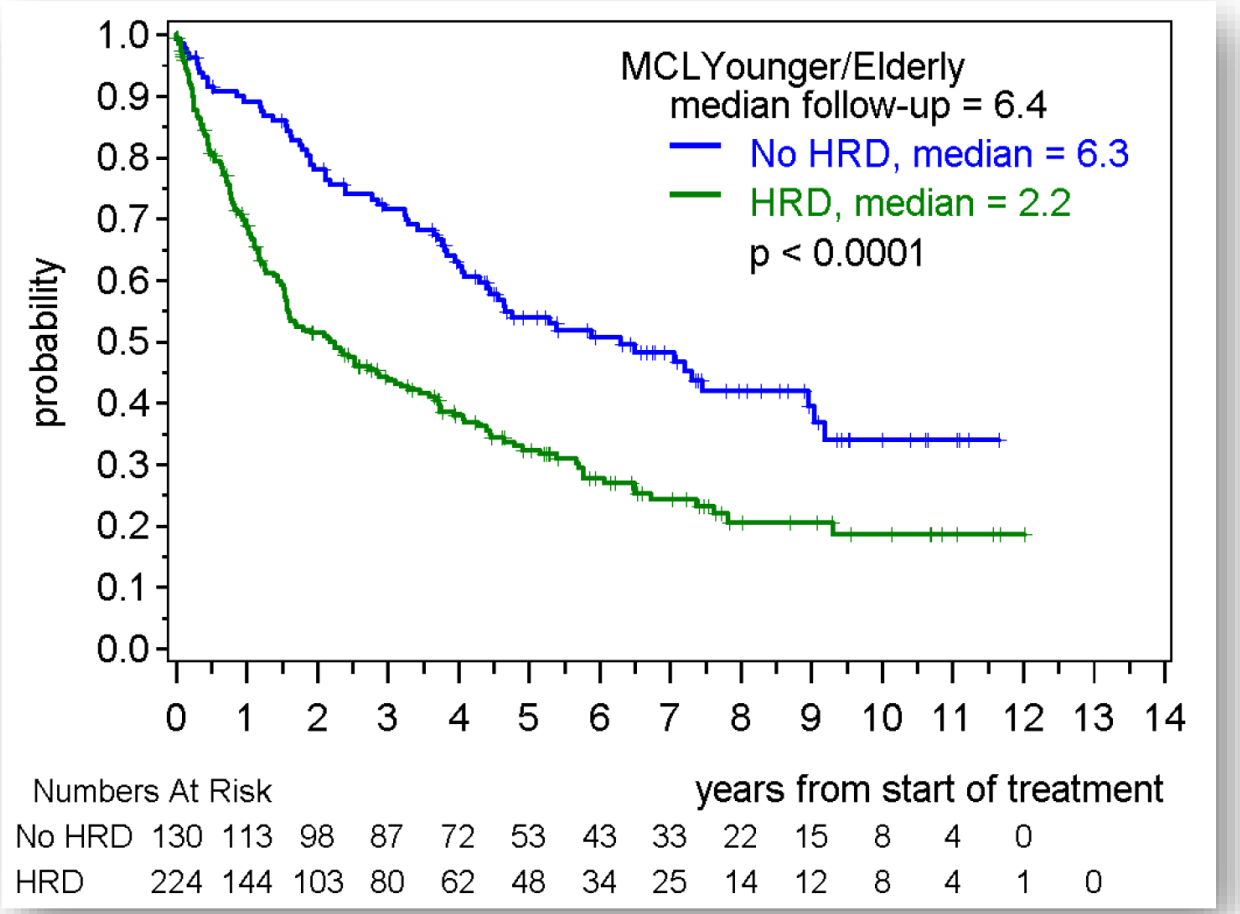
- Work in progress
  - Combination approaches
  - Tailoring of treatment based on individual risk profiles.

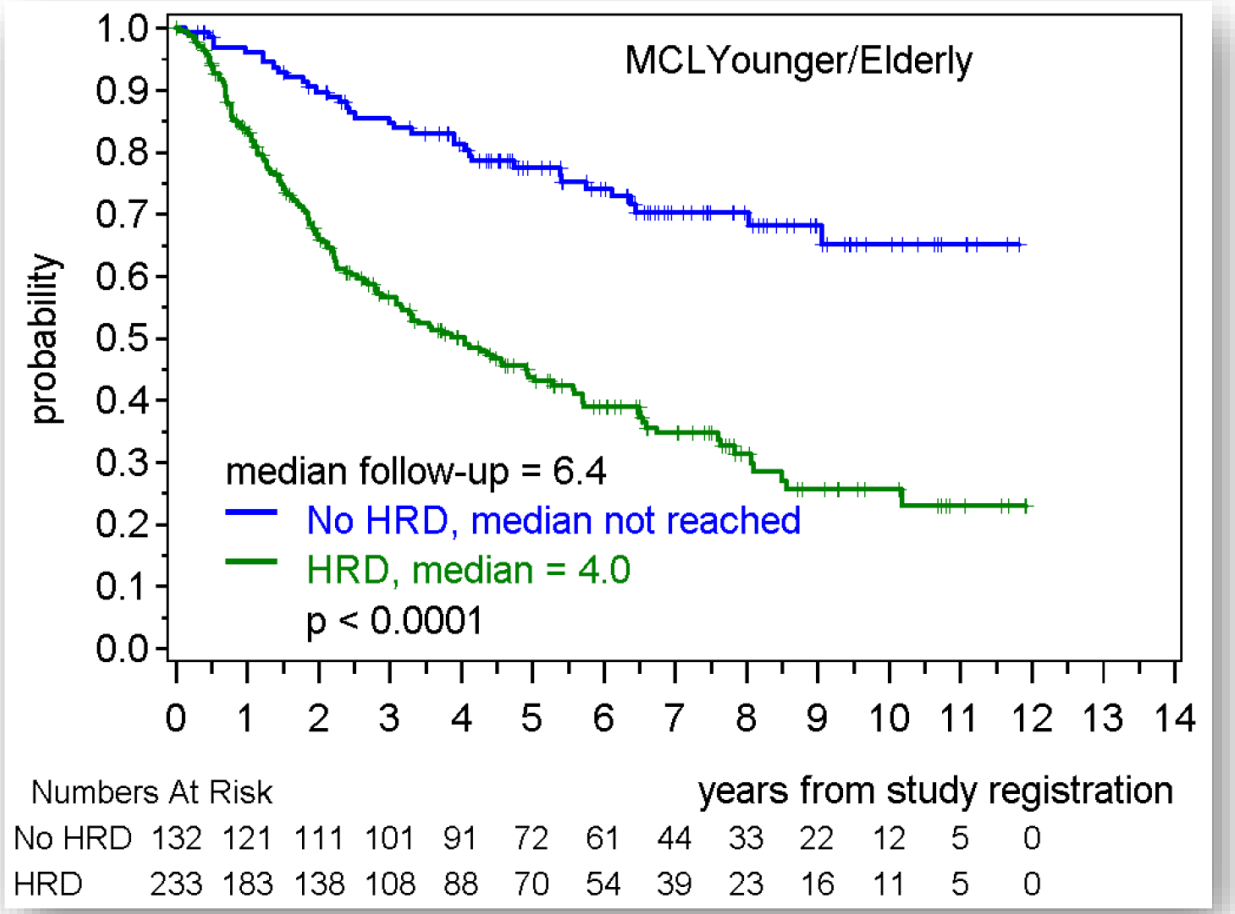
MIPI-C is valid in elderly and younger



Hoster el al., J Clin Oncol, 2016; 34(12):1386-94

Ki67 high OR p53 ICH > 50% or Blastoid morphology

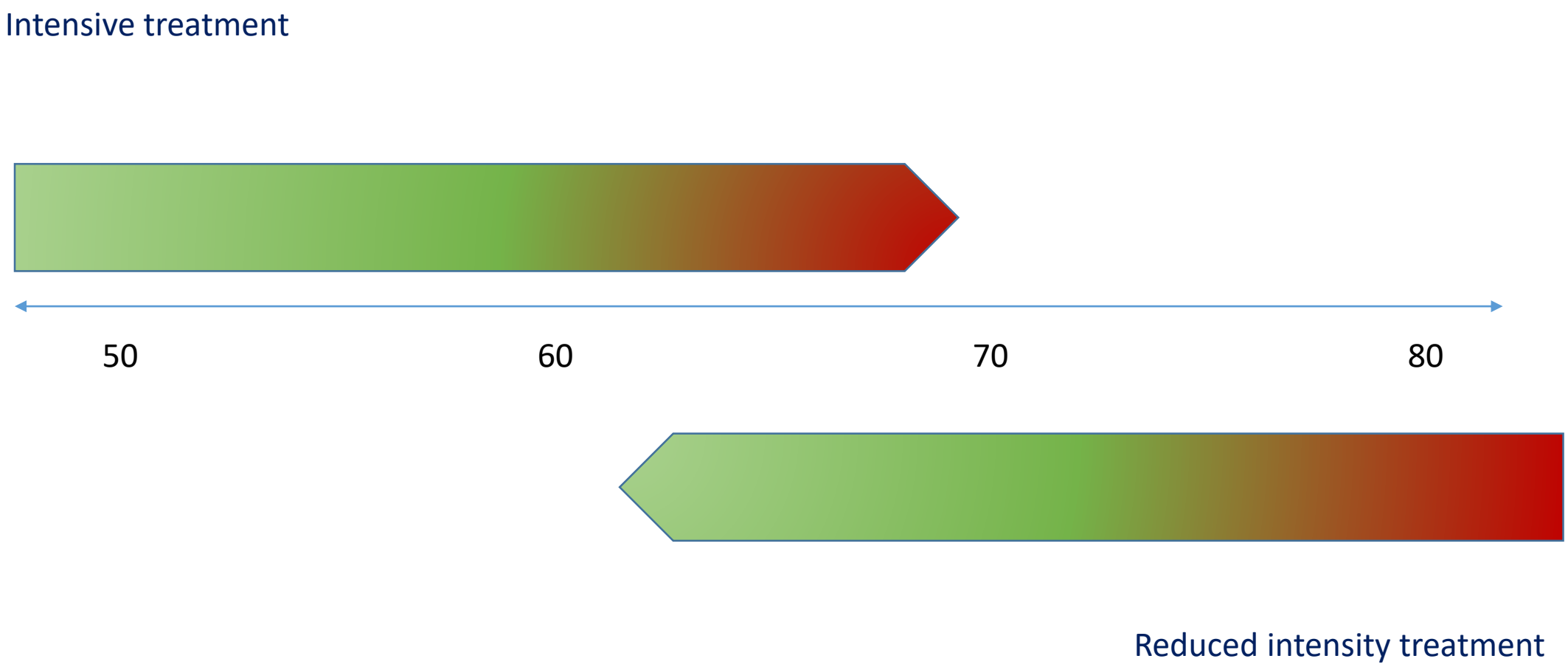




Dreyling et a. Blood (2019) 134 (Supplement_1): 3996.

First line treatment

Transplant in|eligible !?!



Chemoimmunotherapy as SOC

- R-CHOP superior to R-FC
- R maintenance superior to IFN

- RB equivalent to R-CHOP
- Role of Rm after RB not formaly proven, but reasonable evidence

- VR-CAP superior to CHOP

- R-BAC intensive alternative with long term remissions

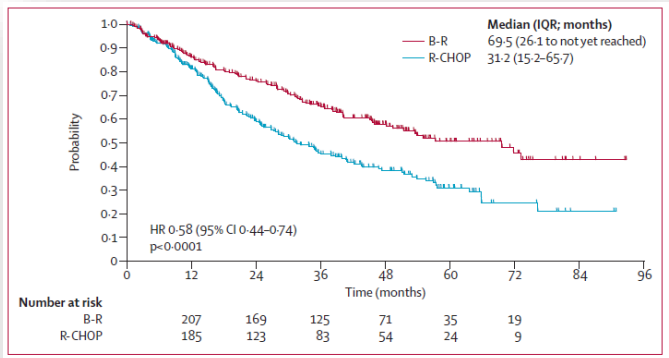


Figure 2: Progression-free survival
B-R=bendamustine plus rituximab. R-CHOP=CHOP plus rituximab.

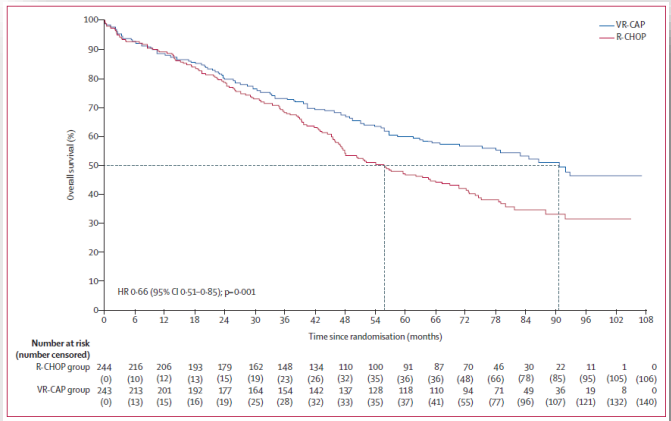
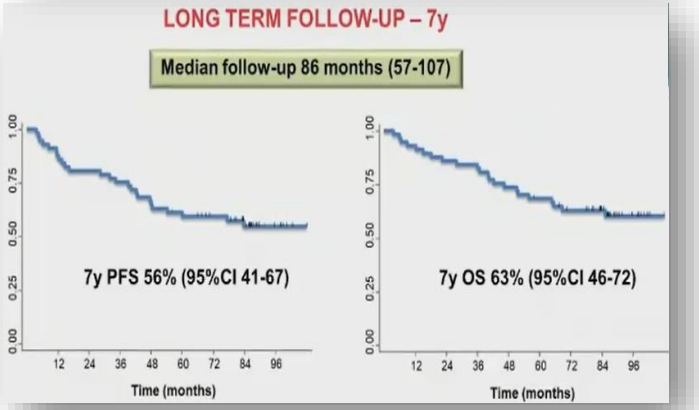


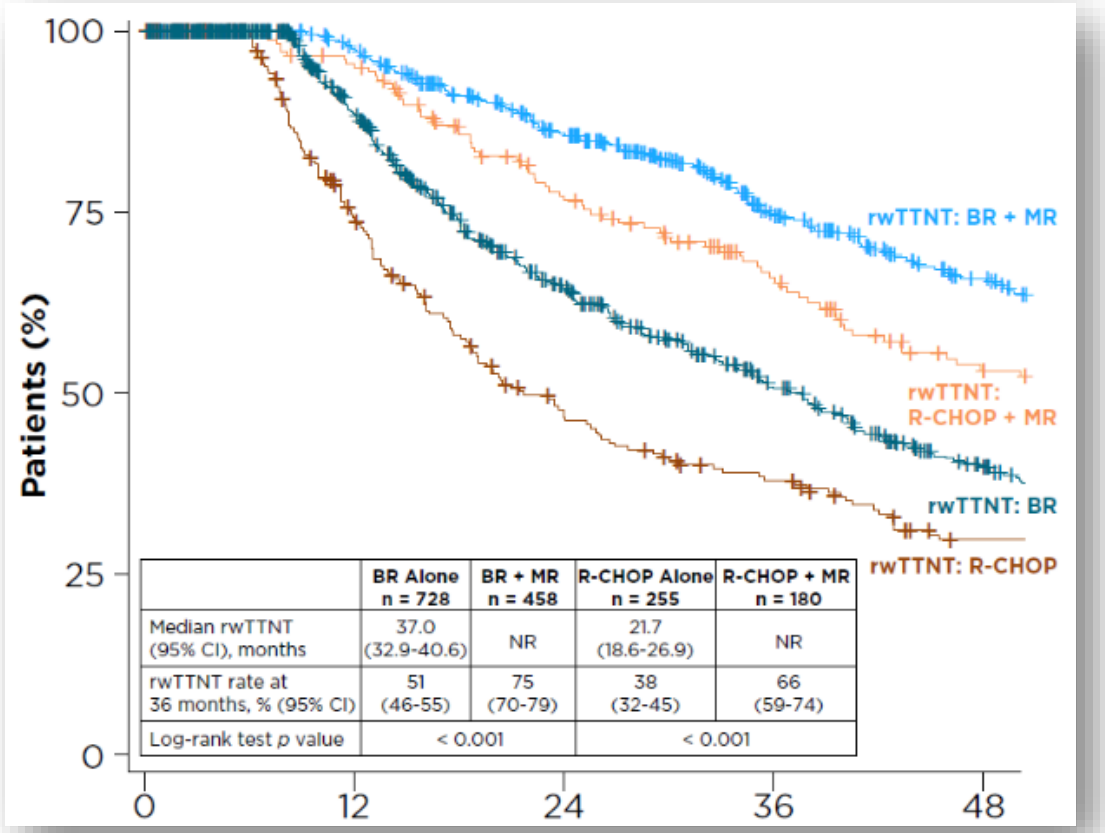
Figure 2: Final analysis of overall survival in the intention-to-treat population
R-CHOP=rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. VR-CAP=bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone. HR=hazard ratio.



Kluin-Nelemans H, et al. N Engl J Med. 2012;367(6):520-31 | Rummel MJ, et al. Lancet. 2013;381(9873):1203-10 | Tisi et al., ASH 2021; abstract 384 |

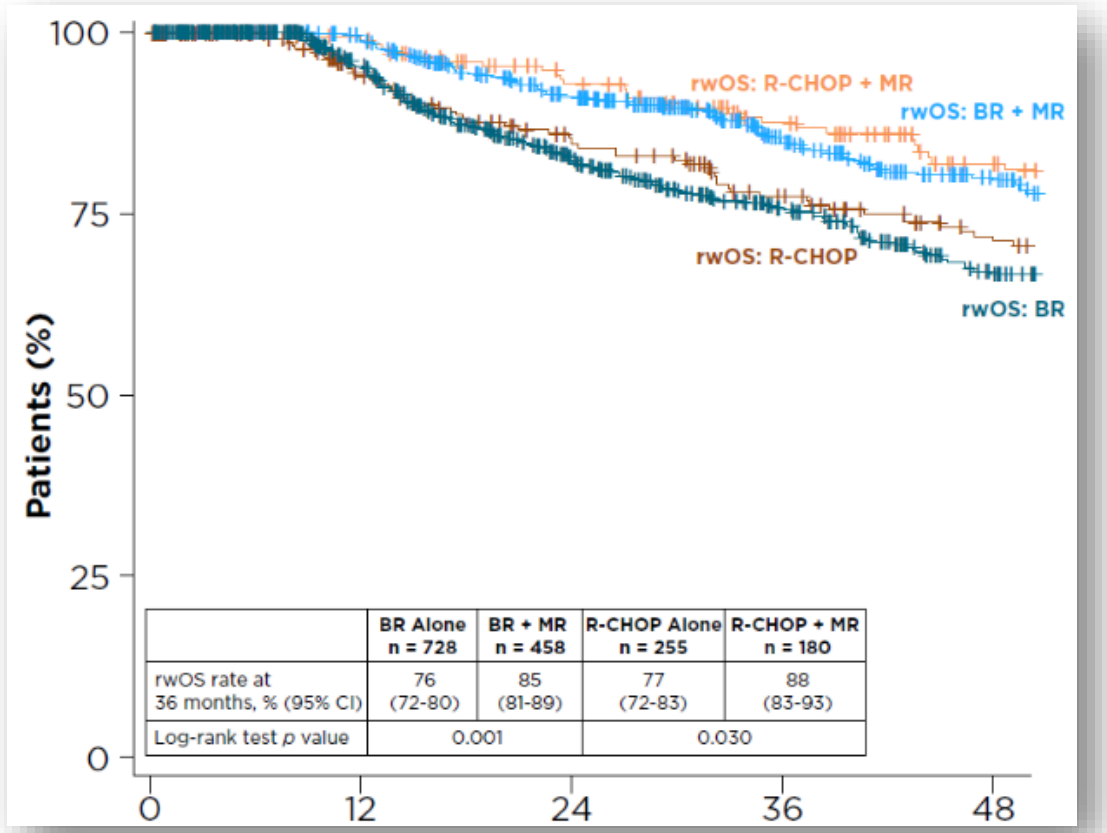
Maintenance rituximab (MR) after first-line BR or R-CHOP in patients with MCL from a large US real-world cohort

Real world TTNT



	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	

Real world OS

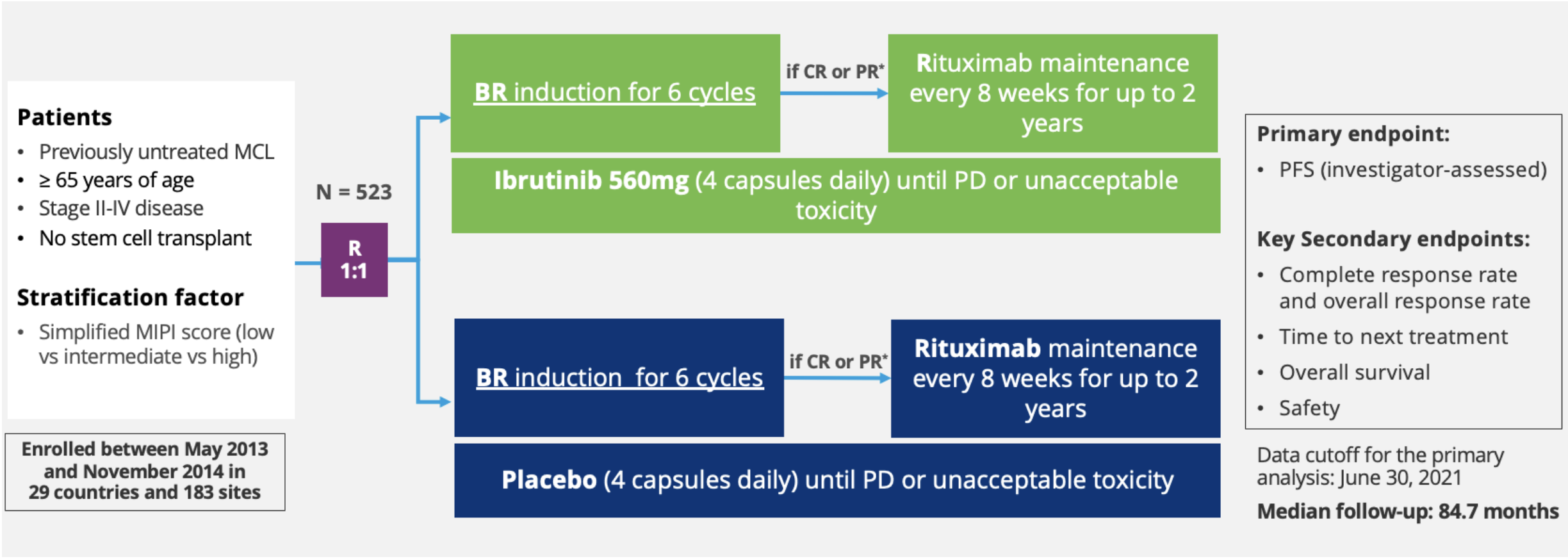


	BR Alone n = 728	BR + MR n = 458	R-CHOP Alone n = 255	R-CHOP + MR n = 180
rwOS rate at 36 months, % (95% CI)	76 (72-80)	85 (81-89)	77 (72-83)	88 (83-93)
Log-rank test *p* value	0.001		0.030	

Salles et al., EHA 2021 EP785 (poster presentation)

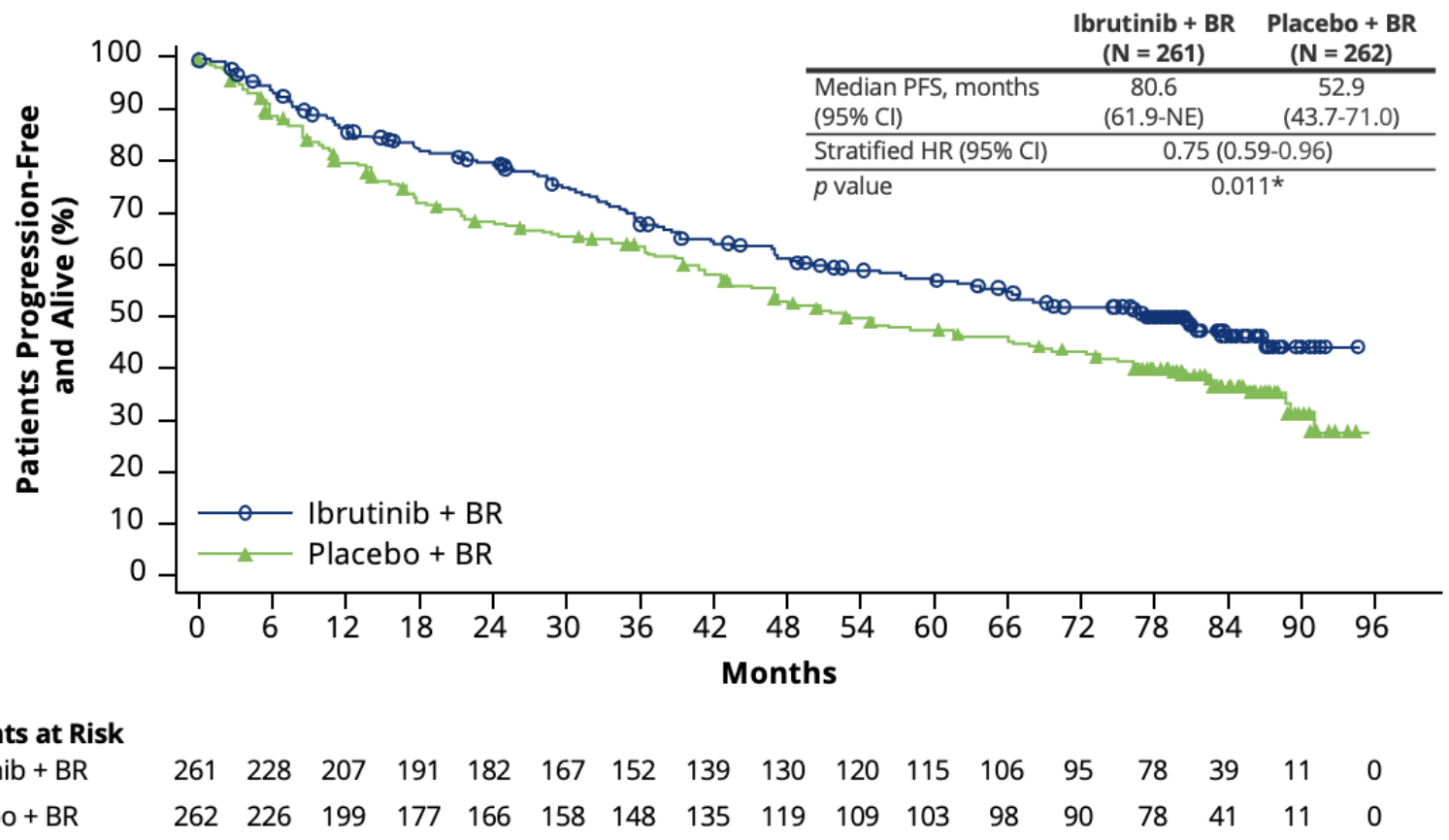
MR was associated with improved rwTTNT and rwOS with both BR and R-CHOP

SHINE - Trial Design



Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

PFS



	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*	

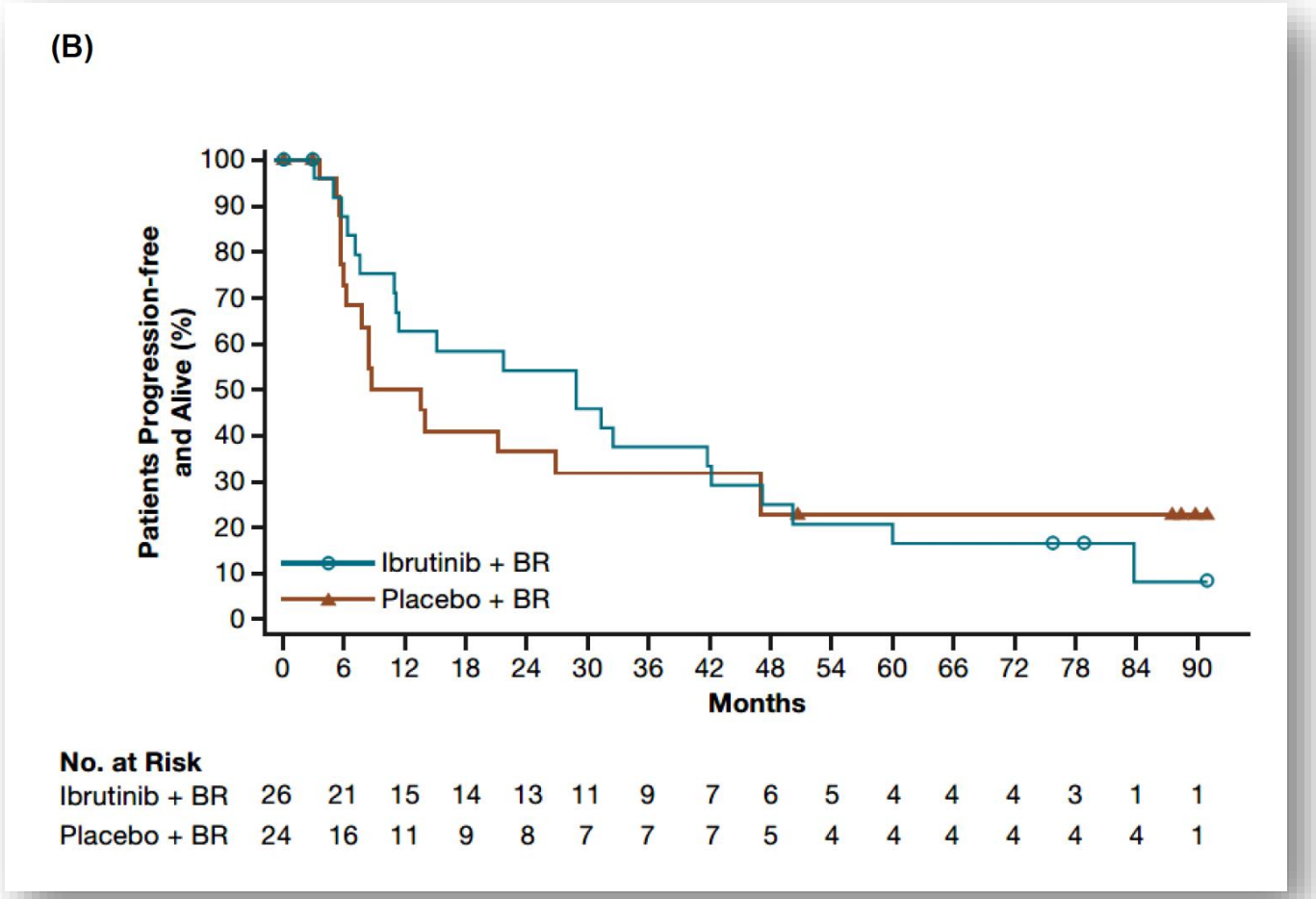
Patients at Risk

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 combined with BR and R maintenance demonstrated **a 25% reduction in the relative risk of disease progression or death** versus BR and R maintenance
- **Significant improvement in median PFS:** 80.6 month (6.7 years) versus 52.9 months (4.4 years) **(Δ=2.3 years)**

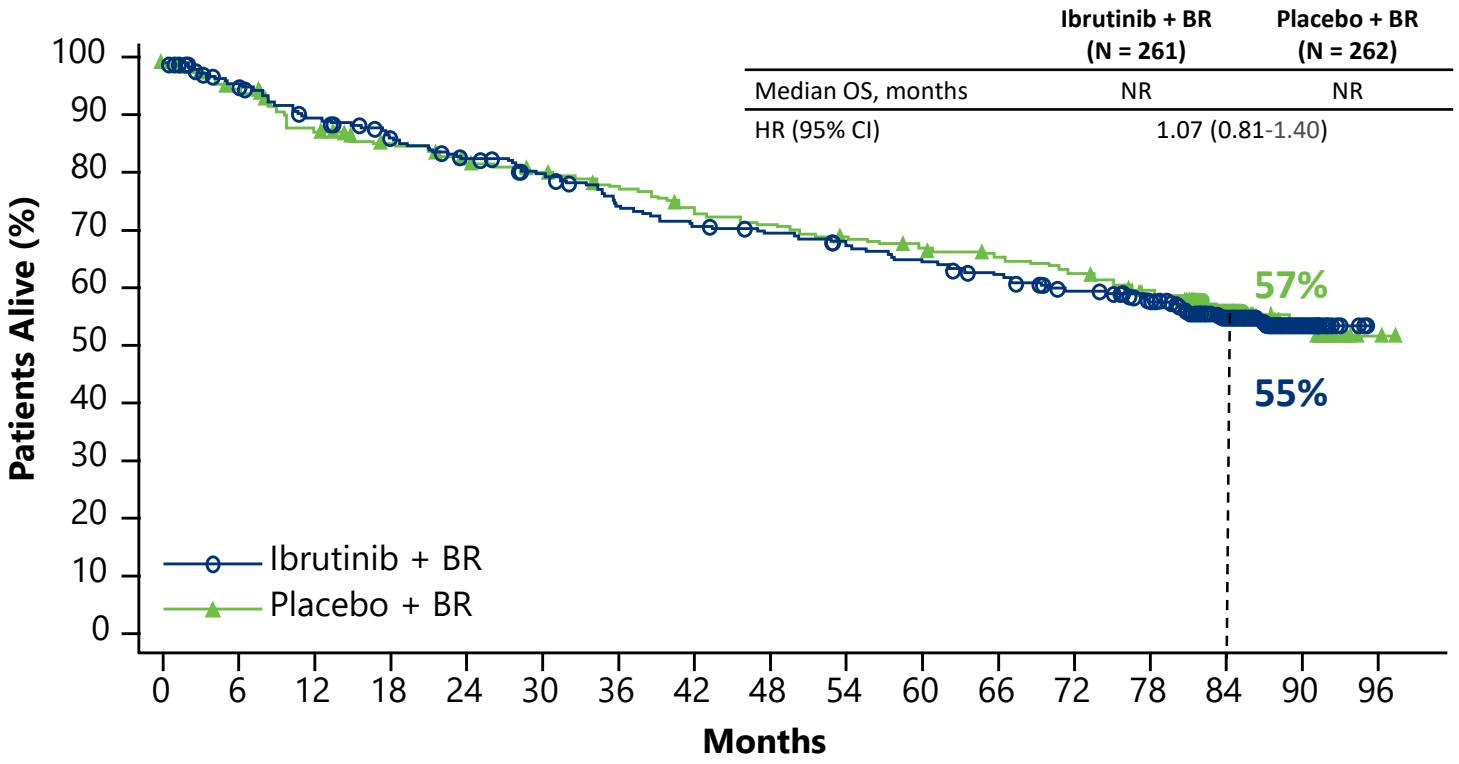
Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

PFS in high risk patients



Wang et al., NEJM, 2022, suppl

Overall Survival Similar in Both Arms



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	30 (11.5%)	54 (20.6%)
Death due to TEAEs*	28 (10.7%)	16 (6.1%)
Death during post-treatment follow-up period excluding PD	46 (17.6%)	37 (14.1%)
Total deaths	**104 (39.8%)**	**107 (40.8%)**

*The most common Grade 5 TEAE was infections in the ibrutinib and placebo arms: 9 vs 5 patients. Grade 5 TEAE of cardiac disorders in 3 vs 5 patients, respectively.

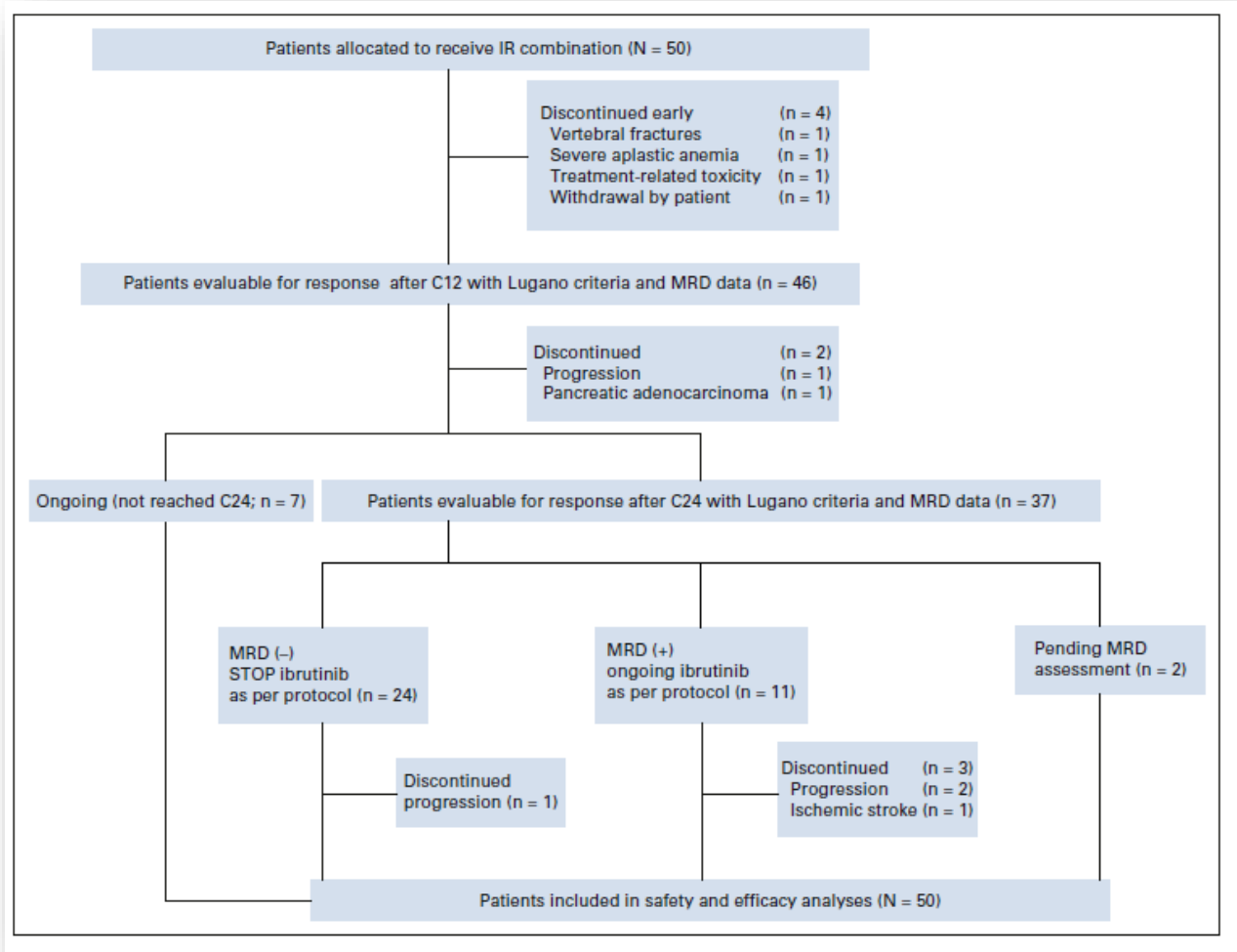
NR, not reached.

Wang et al., EHA 2022; S209 (oral presentation; Wang et al., N Engl J Med. 2022 Jun 3. doi: 10.1056/NEJMoa2201817. Online ahead of print.

Chemofree: Ibrutinib | Rituximab

TABLE 1. Baseline Characteristics of 50 Patients at IMCL-2015 Inclusion

Characteristic	Patients (N = 50)
Median age, years (range)	65 (40-85)
Sex, No. (%)	
Male	33 (66)
Female	17 (44)
ECOG 0-1, No. (%)	50 (100)
Spleen size, cm, median (range)[a]	13 (9-29)
Lymph node size, mm[a]	
No enlarged and no FDG uptake, No. (%)	11 (22)
Longest diameter, median (range)	21 (13-43)
BM involvement	44 (88)
Ann Arbor stage, No. (%)	
I-II	3 (6)
III-IV	47 (94)
WBC count ($\times 10^9$/L), median (range)	12.2 (3.7-126)
PB involvement by flow cytometry, No. (%)	44 of 49 (90)
Hemoglobin (< 110 g/L), No. (%)	3 (6)
Platelet count (< 100 $\times 10^9$/L), No. (%)	4 (8)
Serum LDH (> ULN), No. (%)	4 (8)
Serum B2-microglobulin (> ULN), No. (%)	22 of 45 (49)
MIPI, No. (%)	
Low risk	12 (24)
Intermediate risk	19 (38)
High risk	19 (38)



Giné et al. JCO, 2022, 40:1196-1205

Ibrutinib Rituximab - results

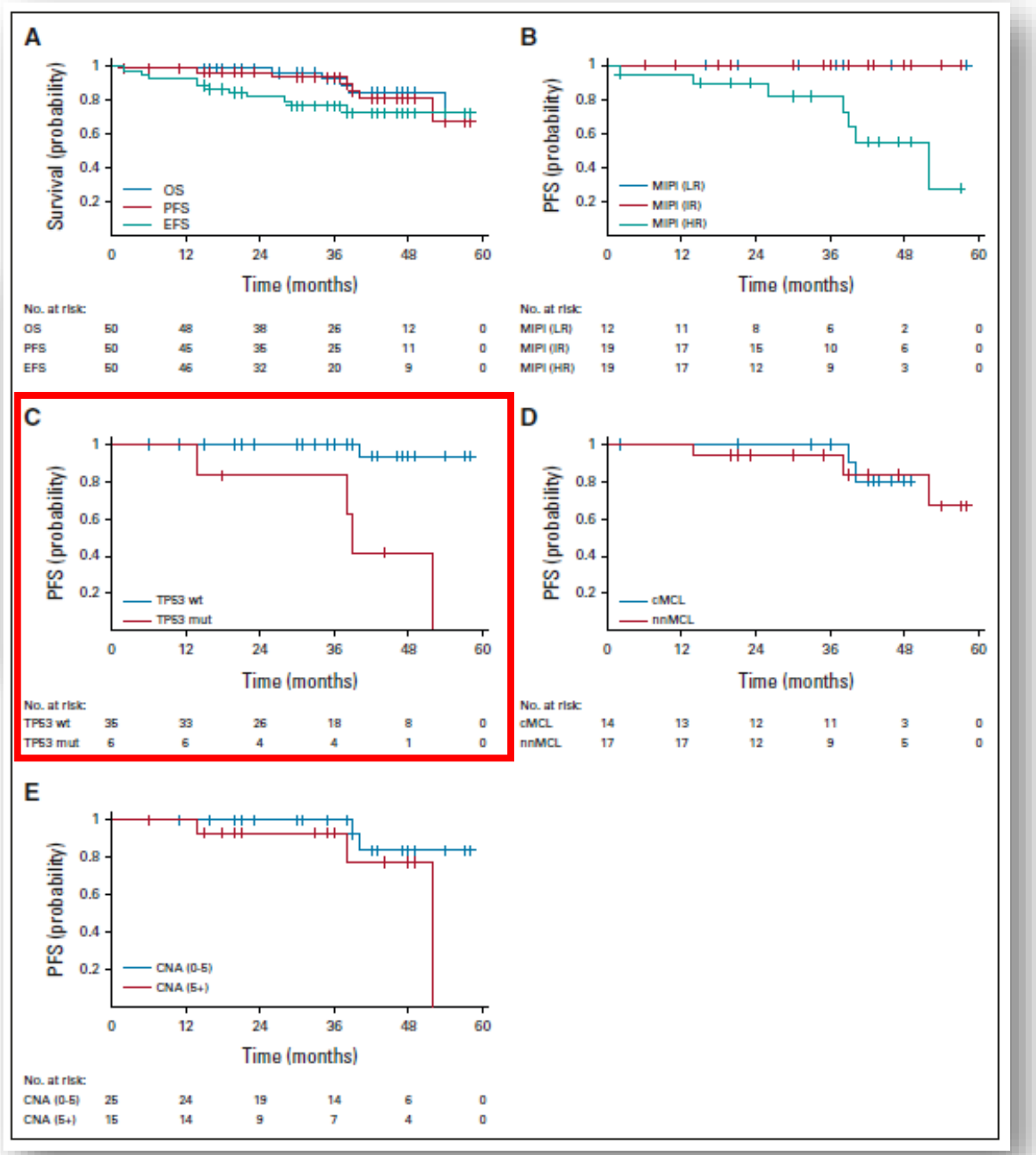
TABLE 3. Responses After 12 Cycles of IR Combination and According to Molecular Subtypes (nnMCL or cMCL) and *TP53* Mutational Status

		Gene Expression Profile L-MCL16		*TP53*	
Response	**All Patients (N = 50)**	**nnMCL (n = 17)**	**cMCL (n = 14)**	**Wild-Type (n = 35)**	**Mutated (n = 6)**
Overall response	42 (84, 74 to 94)	15 (88)	12 (86)	31 (89)	5 (83)
CR	40 (80, 69 to 91)	14 (82)	11 (79)	29 (83)	5 (83)
PR	2 (4, 0 to 9)	1 (6)	1 (7)	2 (6)	—
SD	3 (6, 0 to 10)	1 (6)	1 (7)	3 (8)	—
PD	1 (2, 0 to 6)	1 (6)	—	—	1 (17)
Nonevaluable[a]	4 (8, 0 to 15)	—	1 (7)	1 (3)	—

NOTE. Data are No. (%, 95% CI).

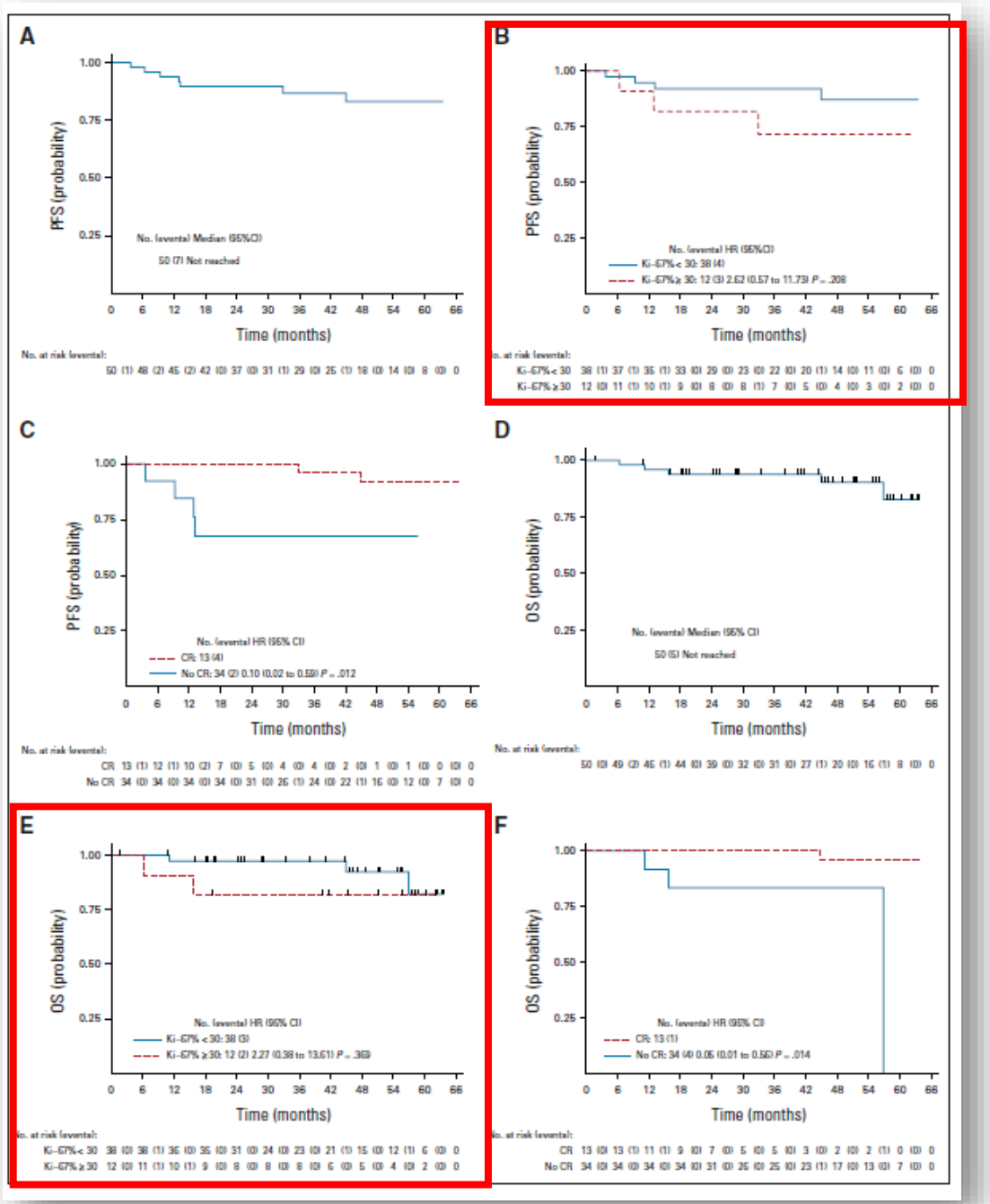
Abbreviations: cMCL, conventional MCL molecular subtype; CR, complete response; IR, ibrutinib, rituximab combination; MCL, mantle cell lymphoma; nnMCL, non-nodal MCL molecular subtype; PD, progressive disease; PR, partial response; SD, stable disease.

[a]Four patients were nonevaluable at 12 months of treatment because of treatment discontinuation: severe aplastic anemia, skin rash, and withdrawal consent because of treatment intolerance and unrelated event with vertebral fractures.



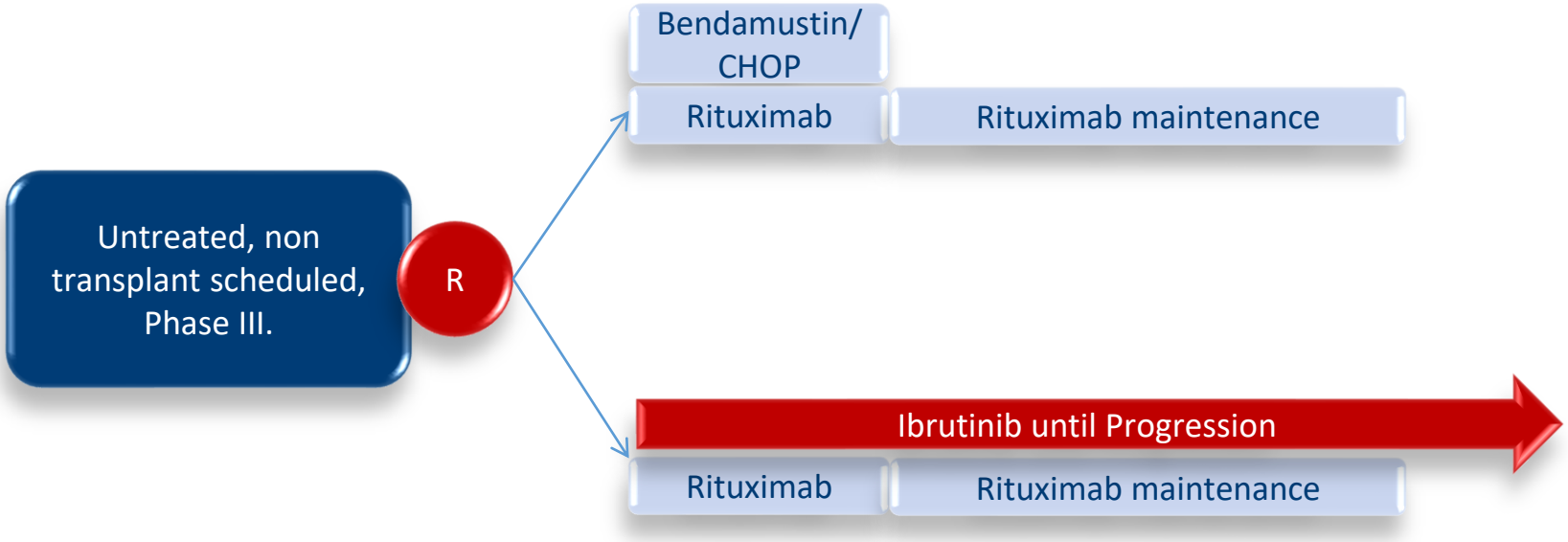
Giné et al. JCO, 2022, 40:1196-1205

MDA-experience



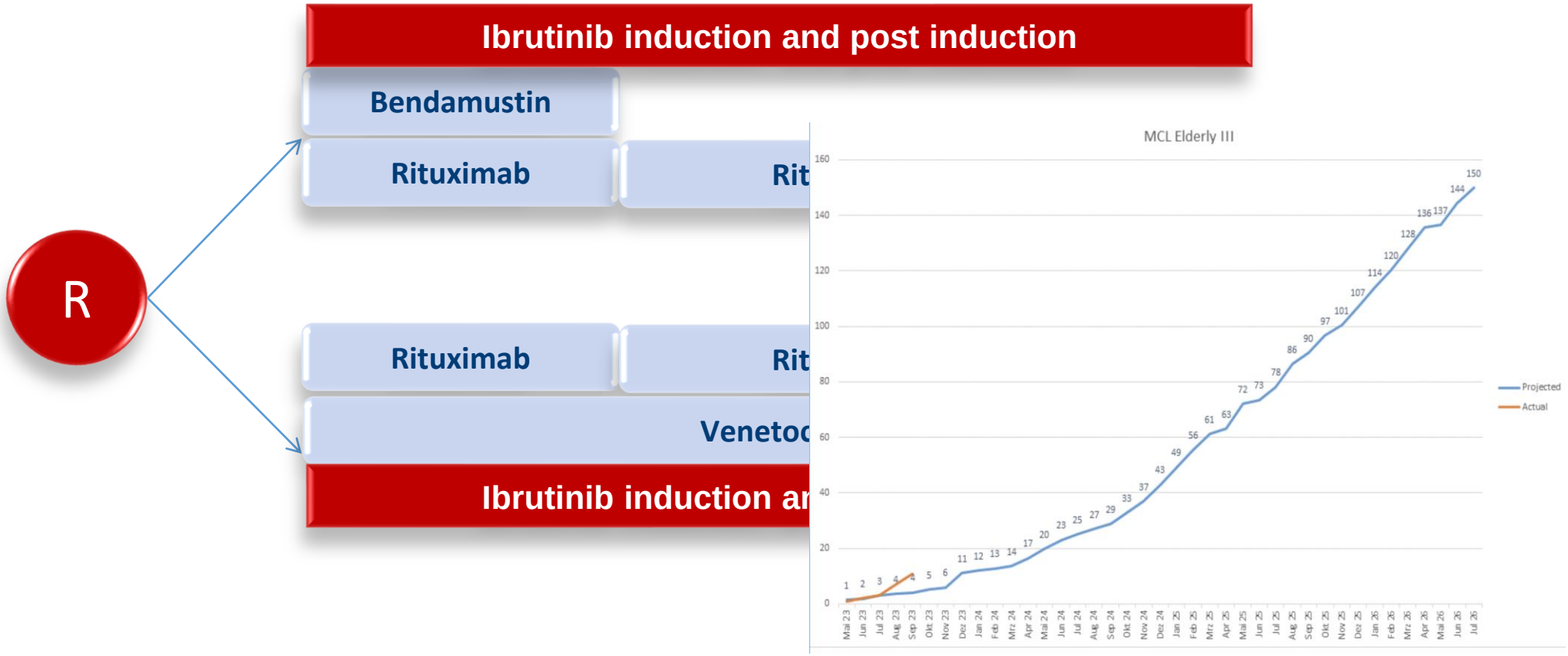
Jain et al, JCO. 2021; 40:202-212

Key Trials: **ENRICH**



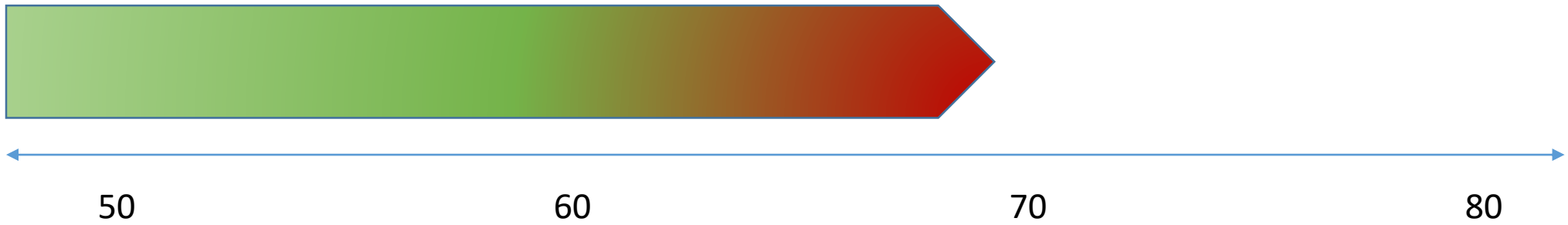
https://doi.org/10.1186/ISRCTN11038174

EMCL-elderly 2023: VIRAL – Phase II



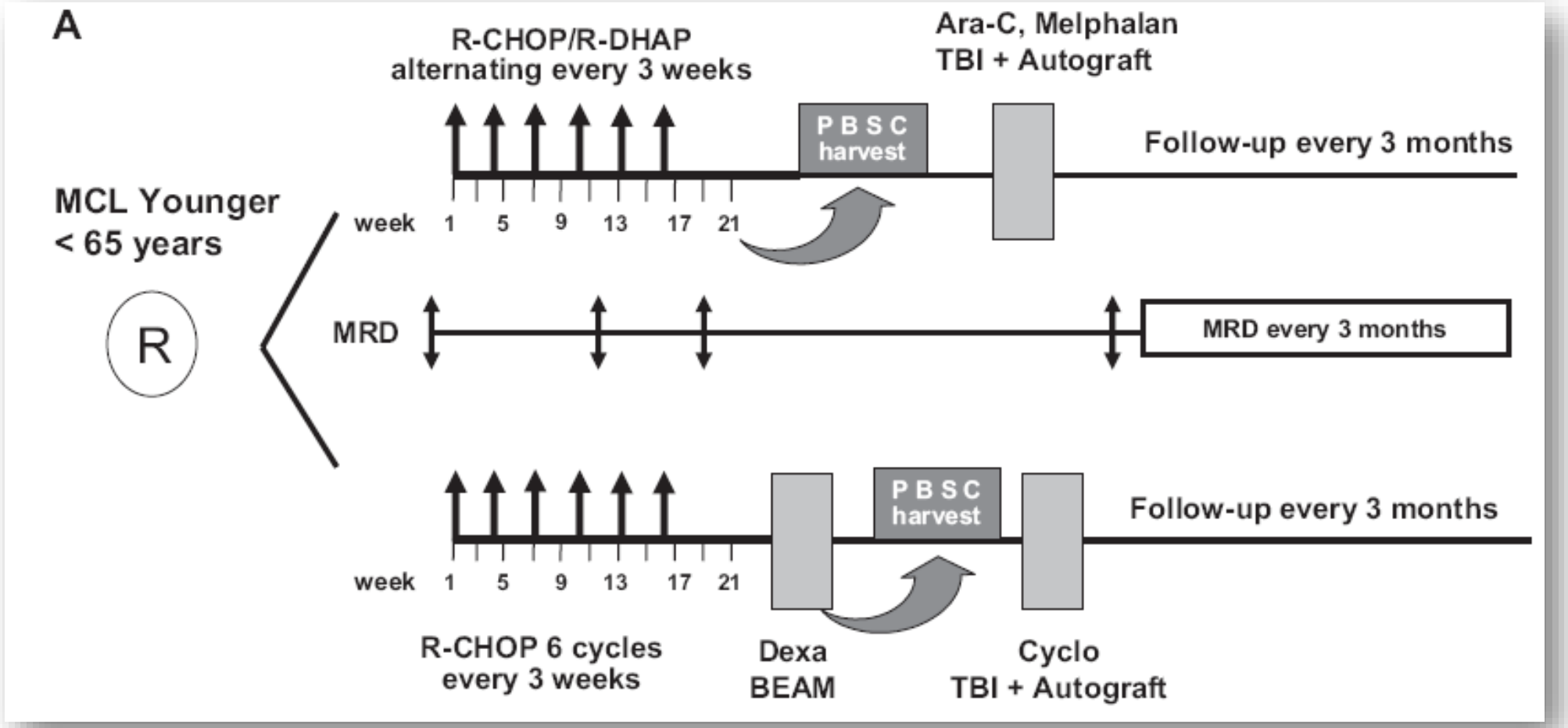
Transplant in|eligible !?!

Intensive treatment



Reduced intensity treatment

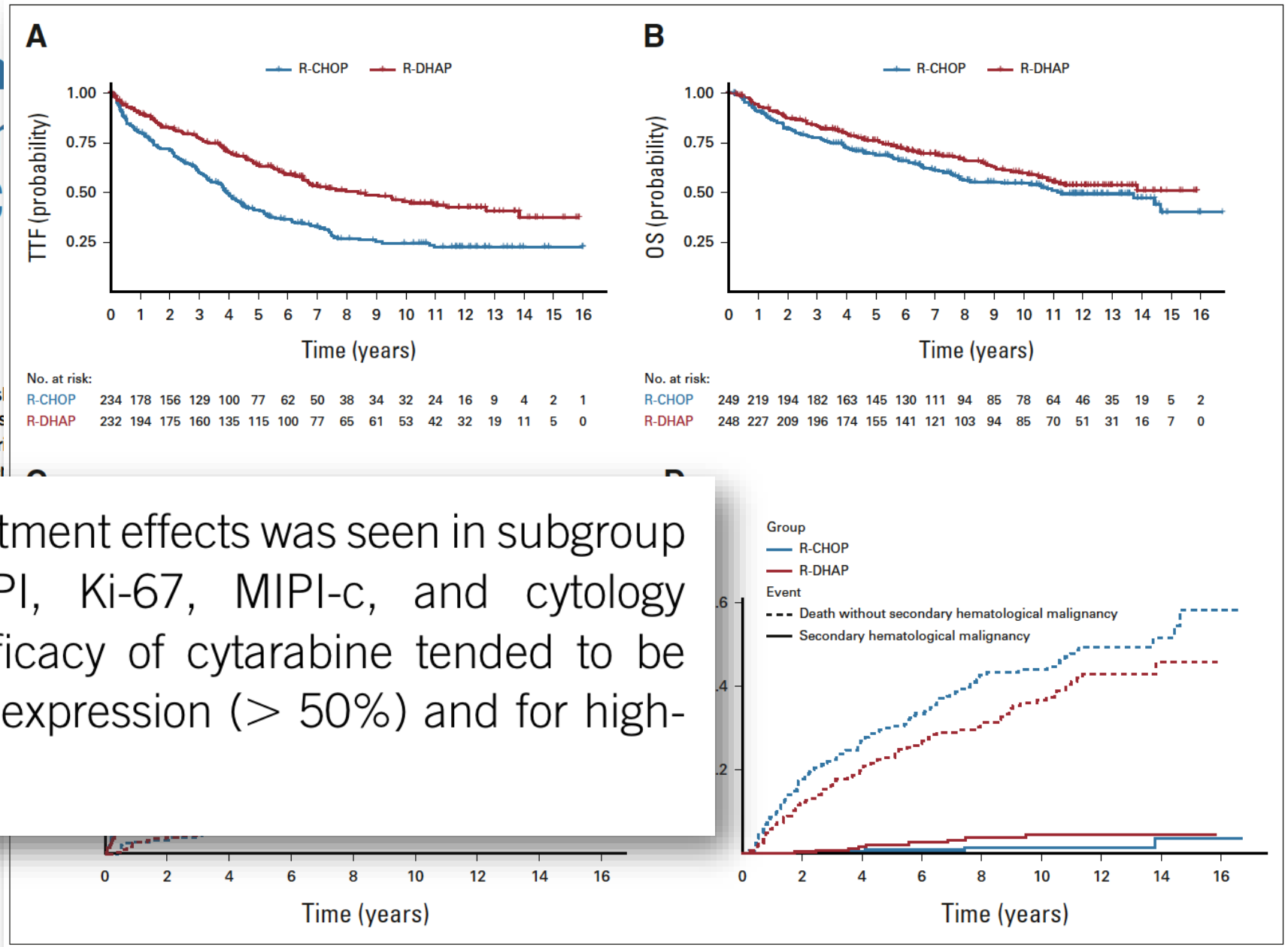
Randomized trial of the EMCL-network



clinical trial updates

High-Dose Cytarabine and Autologous Stem-Cell Transplanta Lymphoma: Long-Term Randomized Mantle C Trial of the European Lymphoma Network

Olivier Hermine, MD, PhD[1,2]; Linmiao Jiang, MSc[3]; Jan Walewsk
Michal Szymczyk, MD[4]; Christiane Pott, MD, PhD[7]; Gilles Salles
Corinne Haioun, MD, PhD[12]; René Olivier Casasnovas, MD[13]; Chri
Lothar Kanz, MD, PhD[17]; Jan Dürig, MD, PhD[18]; Bernd Metzne



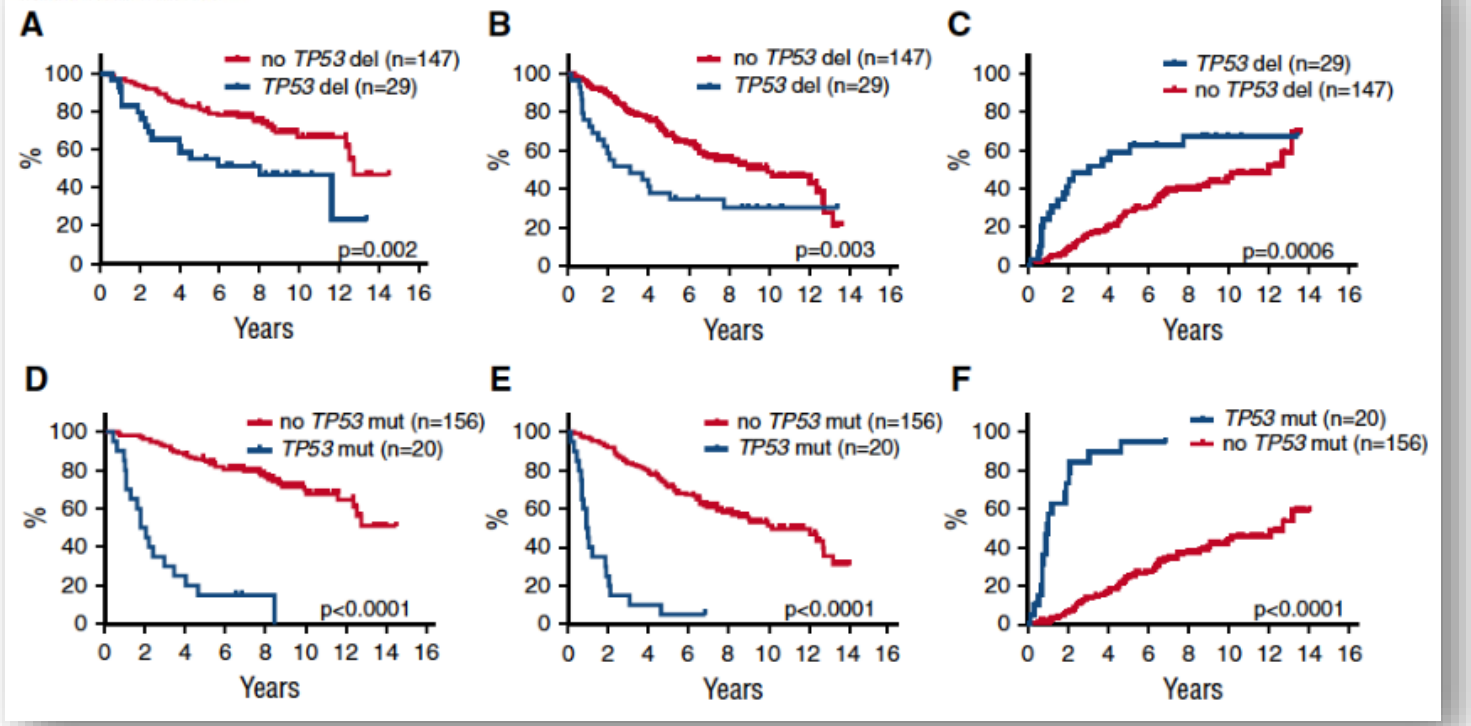
No heterogeneity of treatment effects was seen in subgroup analyses for sex, MIPI, Ki-67, MIPI-c, and cytology (Data Supplement). Efficacy of cytarabine tended to be stronger with high p53 expression (> 50%) and for high-risk MCL.

TP53 mutation in HDT-treated patients

LYMPHOID NEOPLASIA

TP53 mutations identify younger mantle cell lymphoma patients who do not benefit from intensive chemoimmunotherapy

Christian W. Eskelund,[1,2] Christina Dahl,[3] Jakob W. Hansen,[1,2] Maj Westman,[4] Arne Kolstad,[5] Lone B. Pedersen,[1] Carmen P. Montano-Almendras,[1,2] Simon Husby,[1,2] Catja Freiburghaus,[6] Sara Ek,[6] Anja Pedersen,[1,2] Carsten Niemann,[1] Riikka Räty,[7] Peter Brown,[1] Christian H. Geisler,[1] Mette K. Andersen,[4] Per Guldberg,[3] Mats Jerkeman,[8] and Kirsten Grønbæk[1,2]



Eskelund et al., Blood 2017; DOI 10.1182/blood-2017-04-779736; Rule et al. | Haematologica | 2019; 104(5):e211-e214

Including unapproved information in Japan

Alternative induction treatment

REGULAR ARTICLE

blood advances

Rituximab/bendamustine and rituximab/cytarabine induction therapy for transplant-eligible mantle cell lymphoma

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DFCI phase II trial (n=23) (2012-2014)
DFCI off-trial (n=47) (2014-2018)

RB x 3 | RC x 3

WUSTL phase II trial (n=18) (2016-2018)

RB | RC | RB | RC | RB | RC

→ Autologous stem cell transplantation

RB
- Rituximab – 375 mg/m^2, day 1
- Bendamustine – 90 mg/m^2, days 1-2

RC
- Rituximab – 375 mg/m^2, day 1
- Cytarabine – 3 gm/m^2 BID days 1-2*

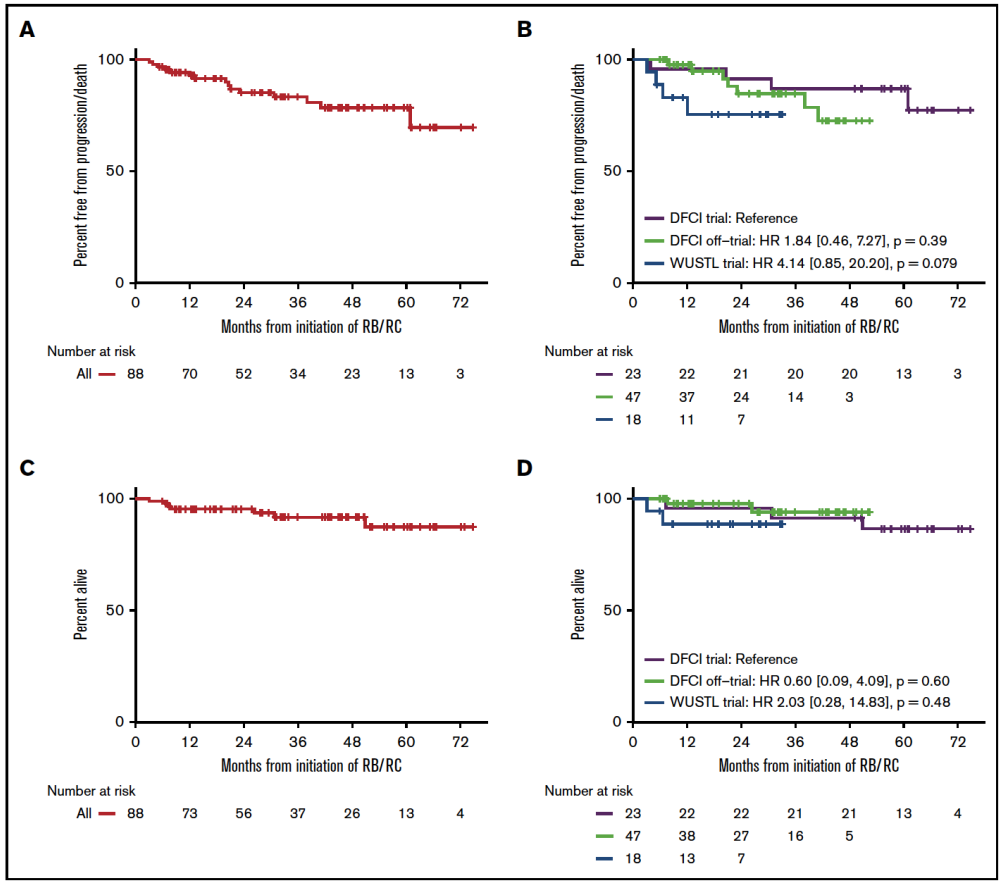
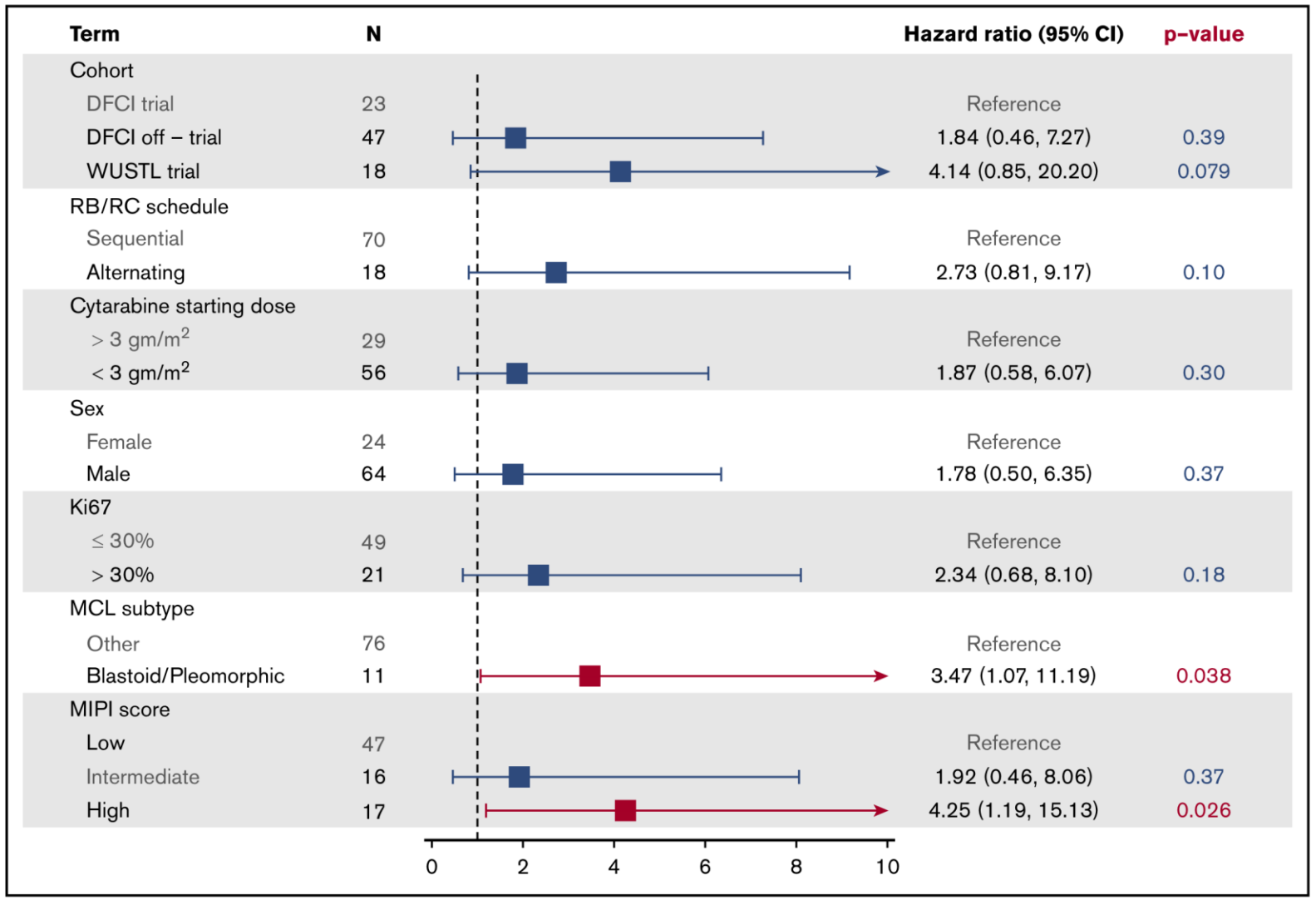


Figure 2. PFS and OS. PFS (A), PFS by cohort (B), OS (C), and OS by cohort (D).

*P.A. and E.J. contributed equally to this study.

The full-text version of this article contains a data supplement.

Alternative induction treatment



De-escalation for induction treatment

REGULAR ARTICLE

blood advances

Bendamustine or high-dose cytarabine-based induction with rituximab in transplant-eligible mantle cell lymphoma

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Adjusted analyses

R-B vs R-CHOP/R-DHAP	97	232	0.83 (0.51-1.34)	.44	0.84 (0.54-1.31)	.44	0.76 (0.44-1.32)	.33
MIPI continuous			2.02 (1.54-2.64)	<.001	2.08 (1.63-2.66)	<.001	2.54 (1.93-3.34)	<.001
R-B vs R-CHOP/R-DHAP	97	169	0.84 (0.51-1.39)	.50	0.87 (0.55-1.38)	.54	0.83 (0.47-1.48)	.54
Blastoid/pleomorphic vs not			2.06 (1.11-3.81)	.021	2.02 (1.14-3.56)	.015	2.06 (1.06-4.02)	.034
R-B vs R-CHOP/R-DHAP	89	129	0.83 (0.48-1.45)	.51	0.78 (0.47-1.31)	.34	0.63 (0.33-1.19)	.15
Ki67 ≥ 30% vs < 30%			1.93 (1.17-3.17)	.010	2.33 (1.49-3.66)	<.001	2.72 (1.59-4.67)	<.001
R-B vs R-CHOP/R-DHAP	89	169	0.82 (0.47-1.42)	.47	0.81 (0.51-1.28)	.36	0.69 (0.36-1.31)	.26
MIPI continuous			2.33 (1.67-3.25)	<.001	2.08 (1.58-2.74)	<.001	2.88 (2.05-4.05)	<.001
Blastoid/pleomorphic vs not			2.01 (1.04-3.90)	.038	1.88 (1.06-3.32)	.030	2.13 (1.05-4.30)	.036
R-B vs R-CHOP/R-DHAP	89	129	0.76 (0.44-1.32)	.33	0.78 (0.47-1.30)	.33	0.63 (0.33-1.19)	.15
MIPI continuous			2.18 (1.55-3.08)	<.001	2.15 (1.59-2.90)	<.001	2.53 (1.78-3.60)	<.001
Ki67 ≥ 30% vs < 30%			1.46 (0.86-2.48)	.16	1.91 (1.20-3.04)	.006	1.95 (1.08-3.51)	.026
R-B vs R-CHOP/R-DHAP	89	114	0.81 (0.47-1.42)	.47	0.76 (0.45-1.28)	.30	0.63 (0.33-1.21)	.16
Ki67 ≥ 30% vs < 30%			1.73 (1.04-2.89)	.035	2.09 (1.32-3.32)	.002	2.51 (1.43-4.42)	.001
Blastoid/pleomorphic vs not			2.01 (1.04-3.89)	.039	1.92 (1.05-3.52)	.035	2.05 (1.02-4.13)	.045
R-B vs R-CHOP/R-DHAP	89	114	0.79 (0.45-1.37)	.40	0.75 (0.45-1.25)	.27	0.65 (0.34-1.24)	.19
MIPI continuous			2.17 (1.53-3.07)	<.001	2.14 (1.57-2.93)	<.001	2.52 (1.76-3.60)	<.001
Ki67 ≥ 30% vs < 30%			1.38 (0.81-2.36)	.24	1.67 (1.03-2.71)	.037	1.82 (1.0-3.31)	.050
Blastoid/pleomorphic vs not			1.90 (0.98-3.71)	.058	1.81 (0.98-3.34)	.057	1.89 (0.93-3.84)	.080

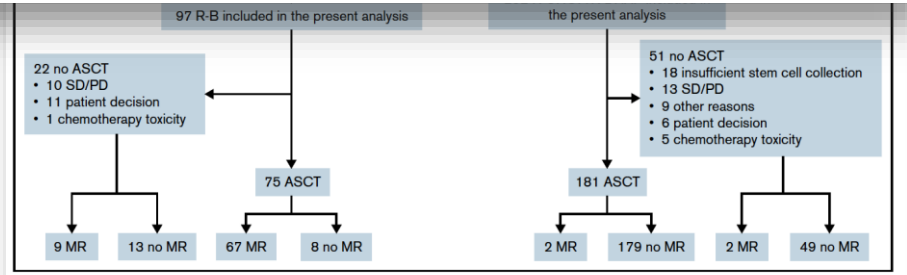


Figure 1. **Patient identification.**

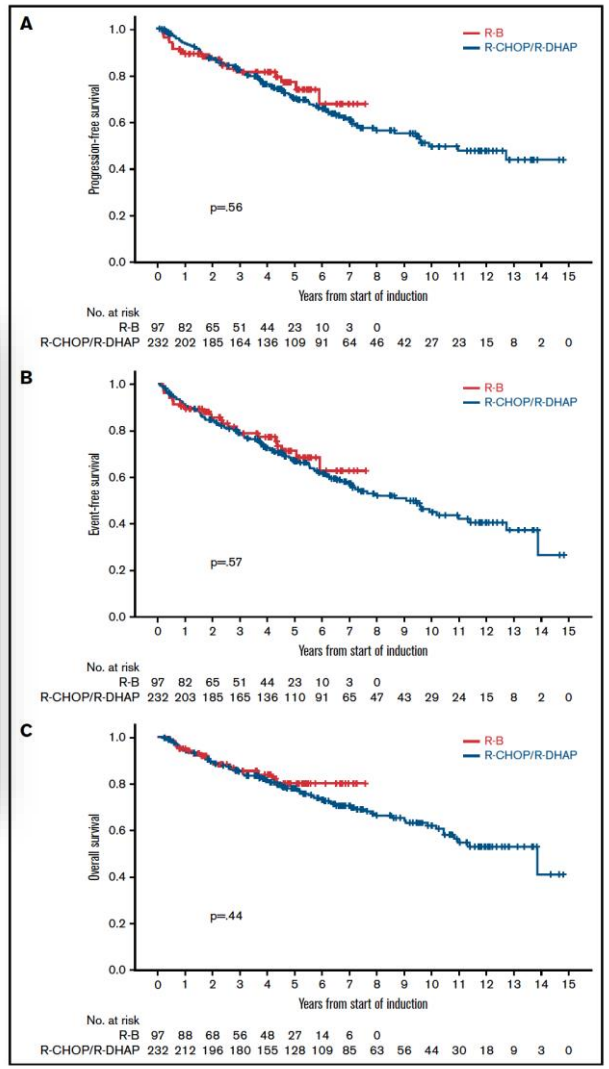


Figure 2. **Crude outcome comparisons between R-B and R-CHOP/R-DHAP.** (A) PFS. (B) EFS. (C) OS.

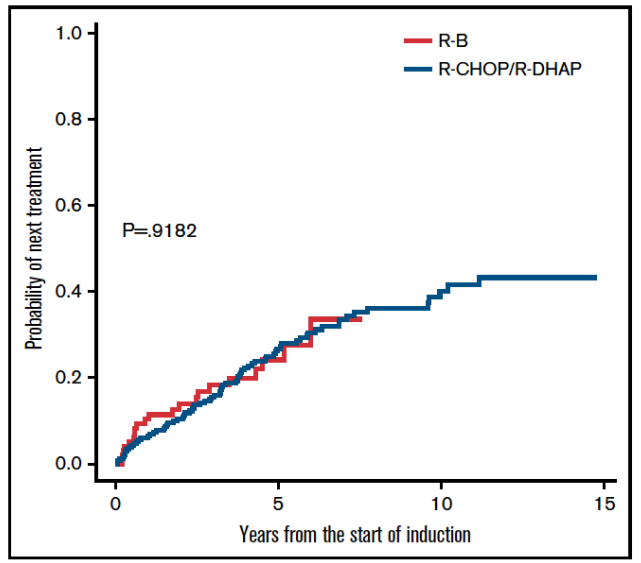


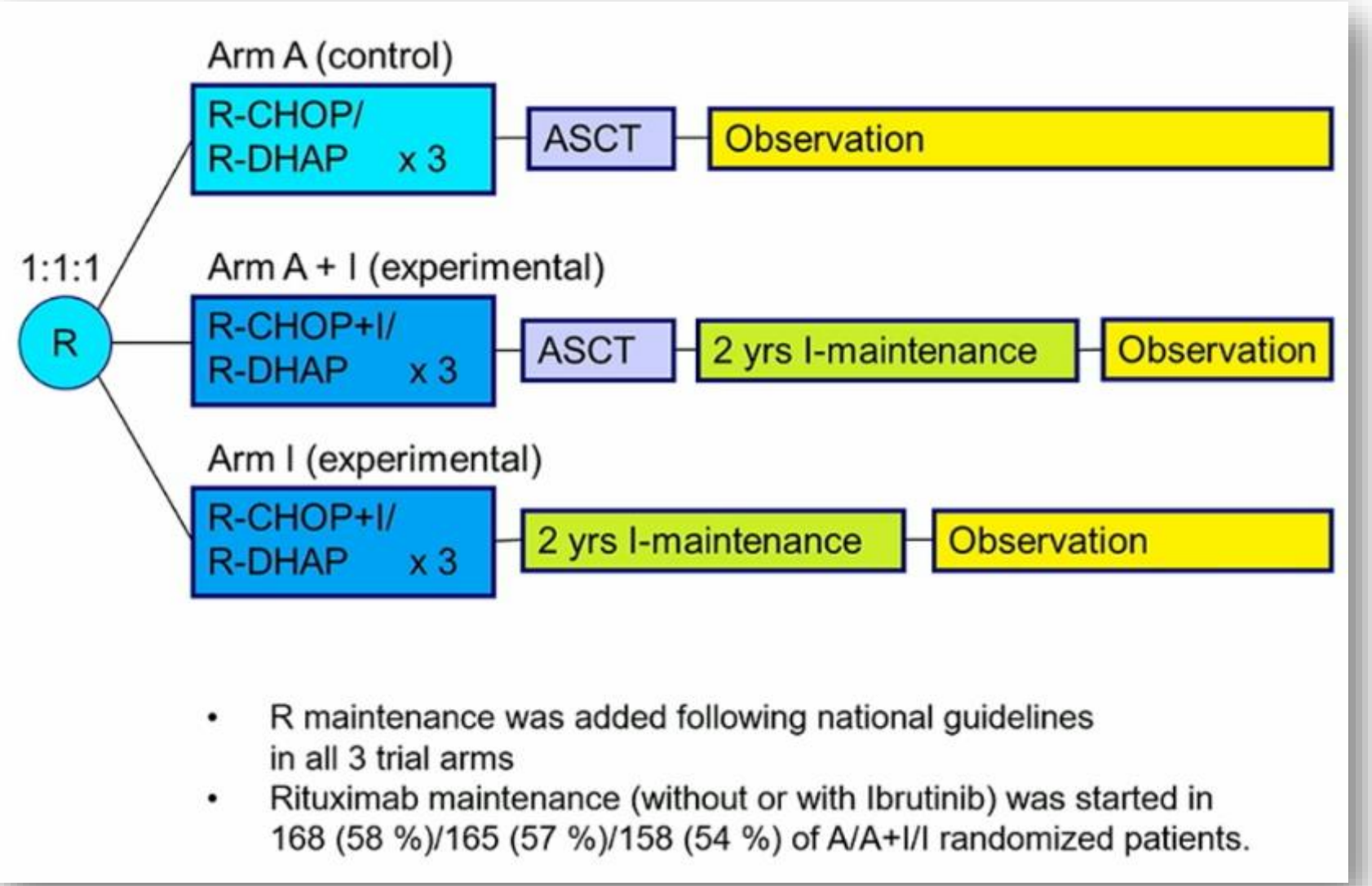
Figure 3. **Time to next treatment comparisons between R-B and R-CHOP/R-DHAP.**

TRIANGLE: study 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



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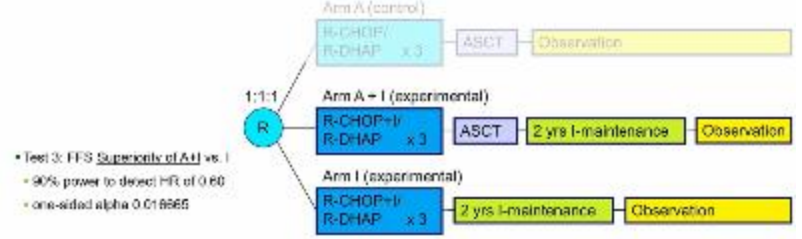
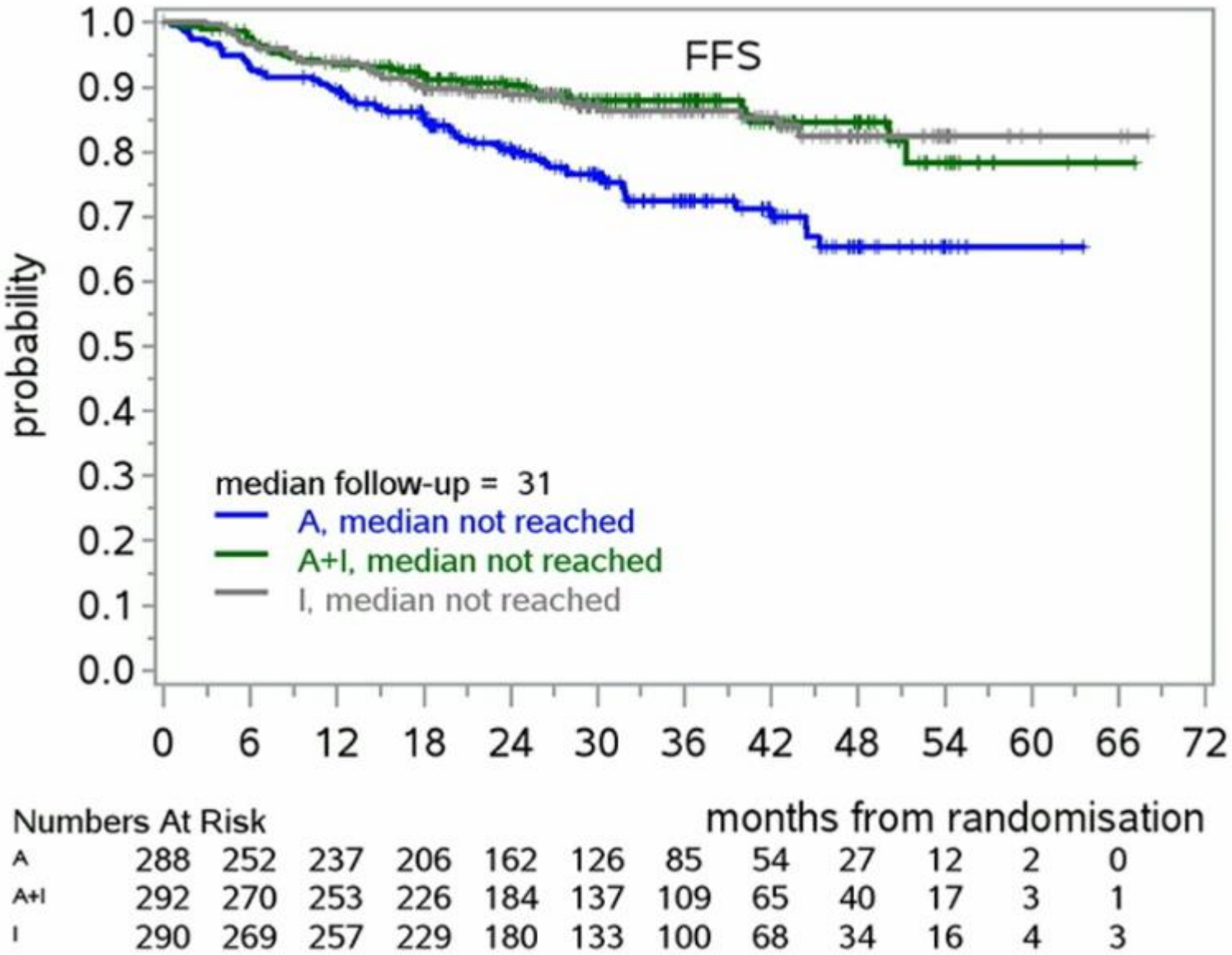
Triangle: A+I vs I





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

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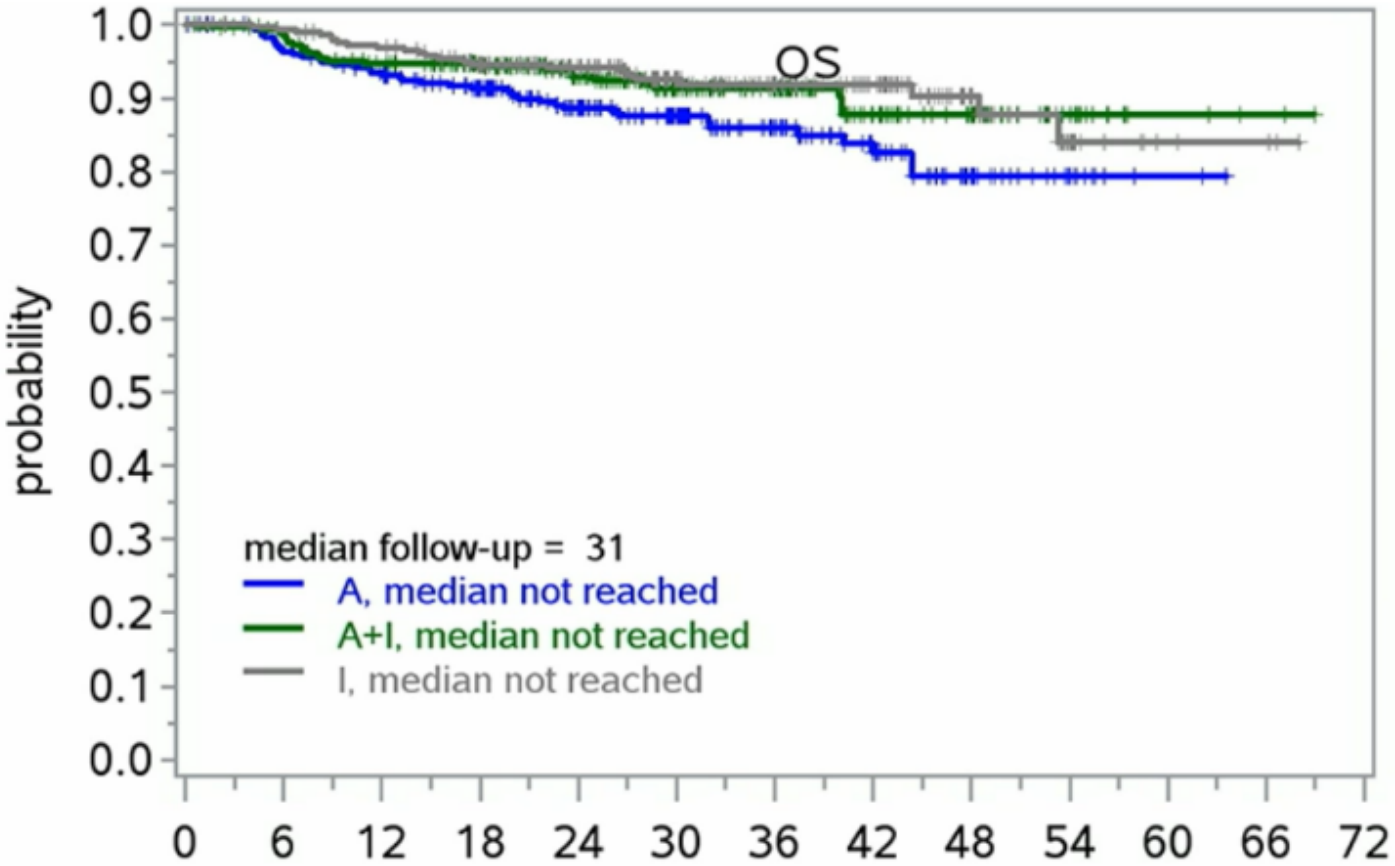
Triangle: overall survival



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

- 3-year OS:
  - A: 86% (MCL Younger exp.: 84%)
  - A+I: 91%
  - I: 92%
- Too early to evaluate statistical significance

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

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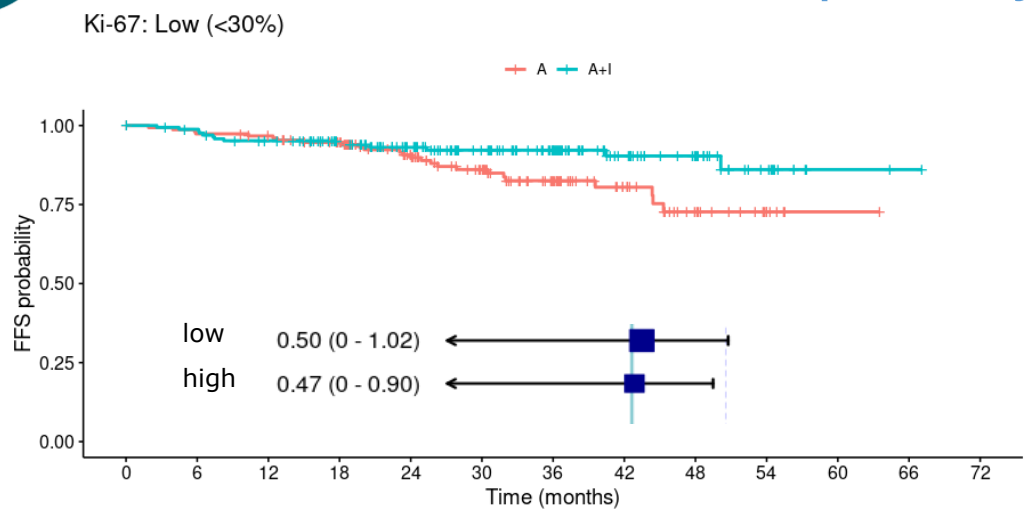
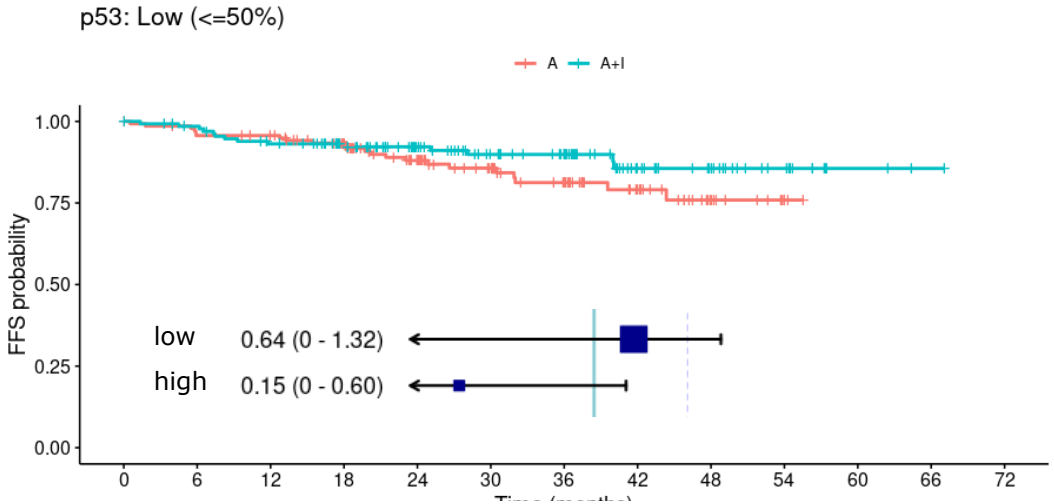
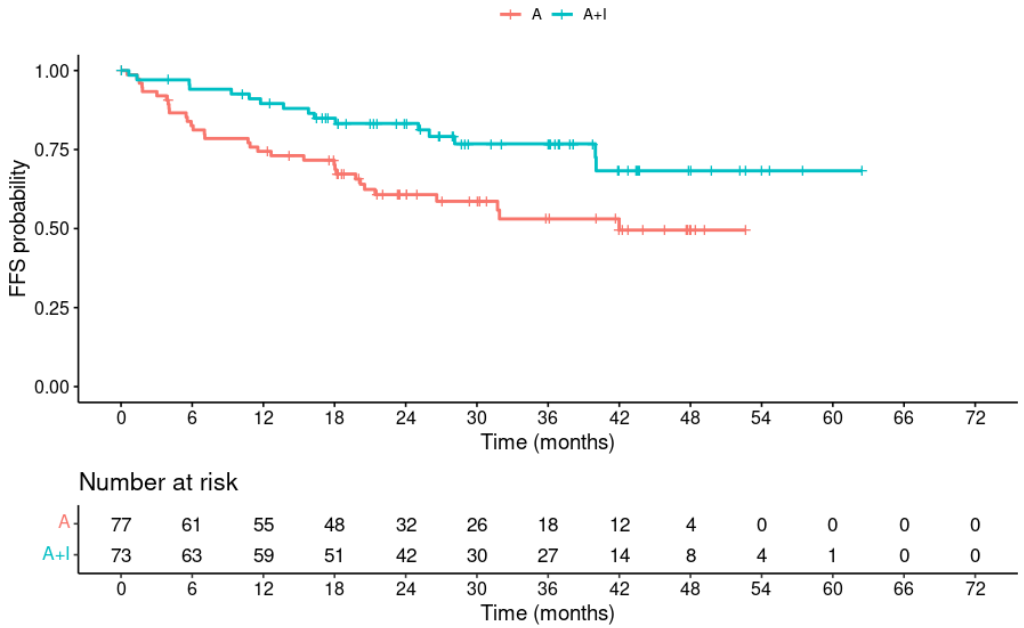
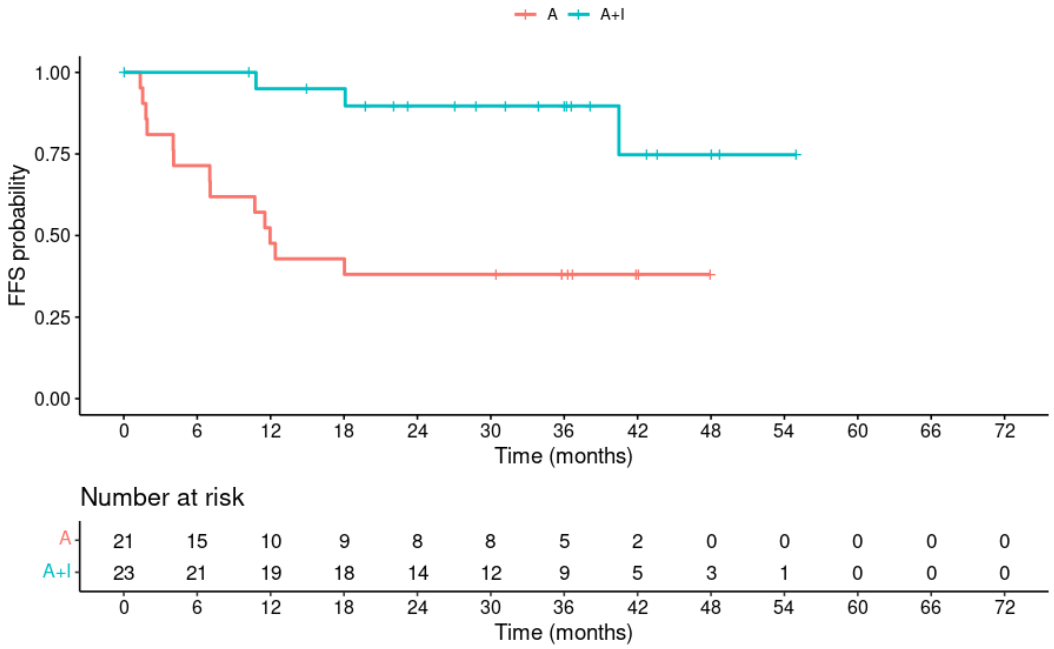
TRIANGLE: FFS Superiority of A+I vs. A



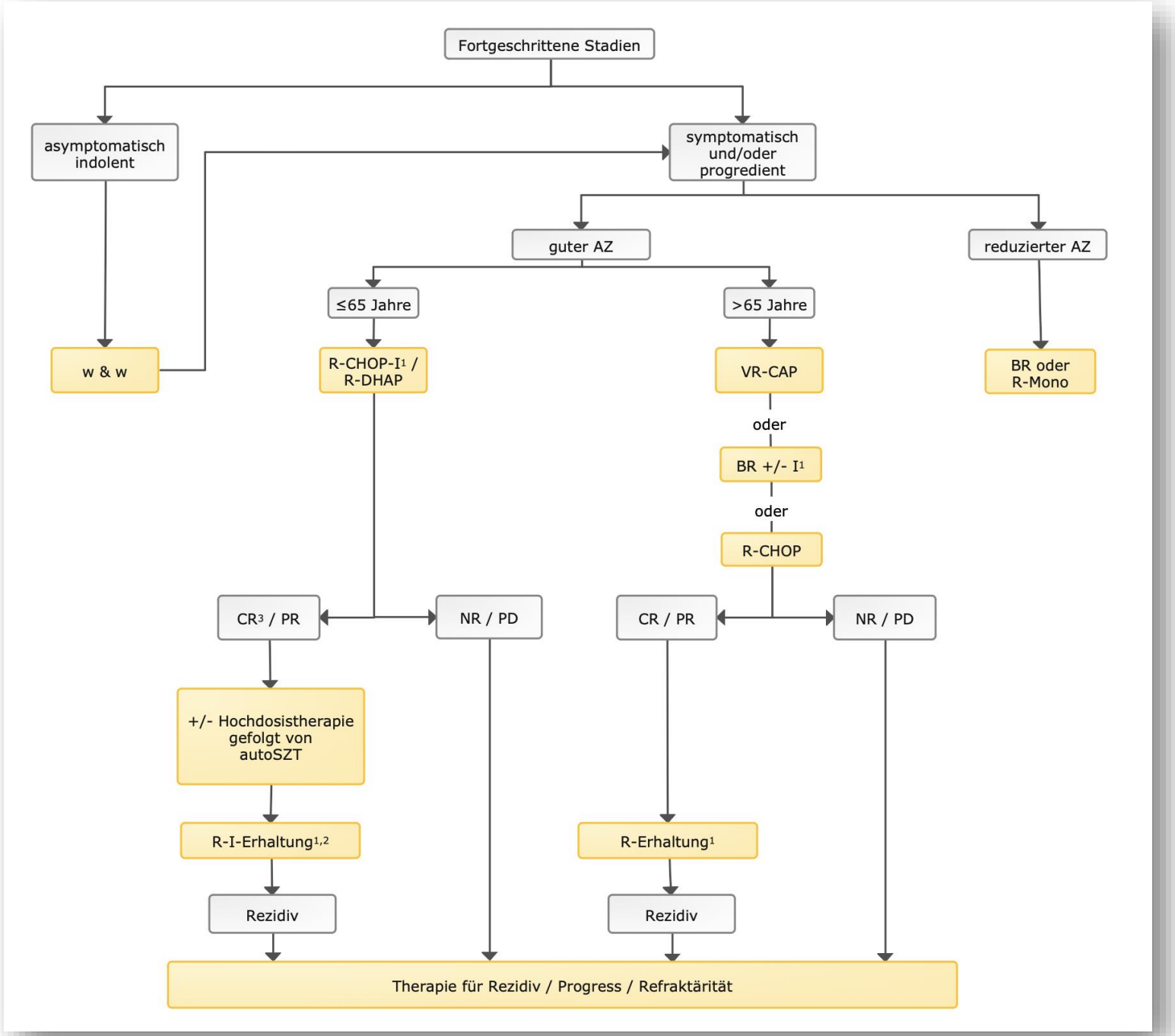




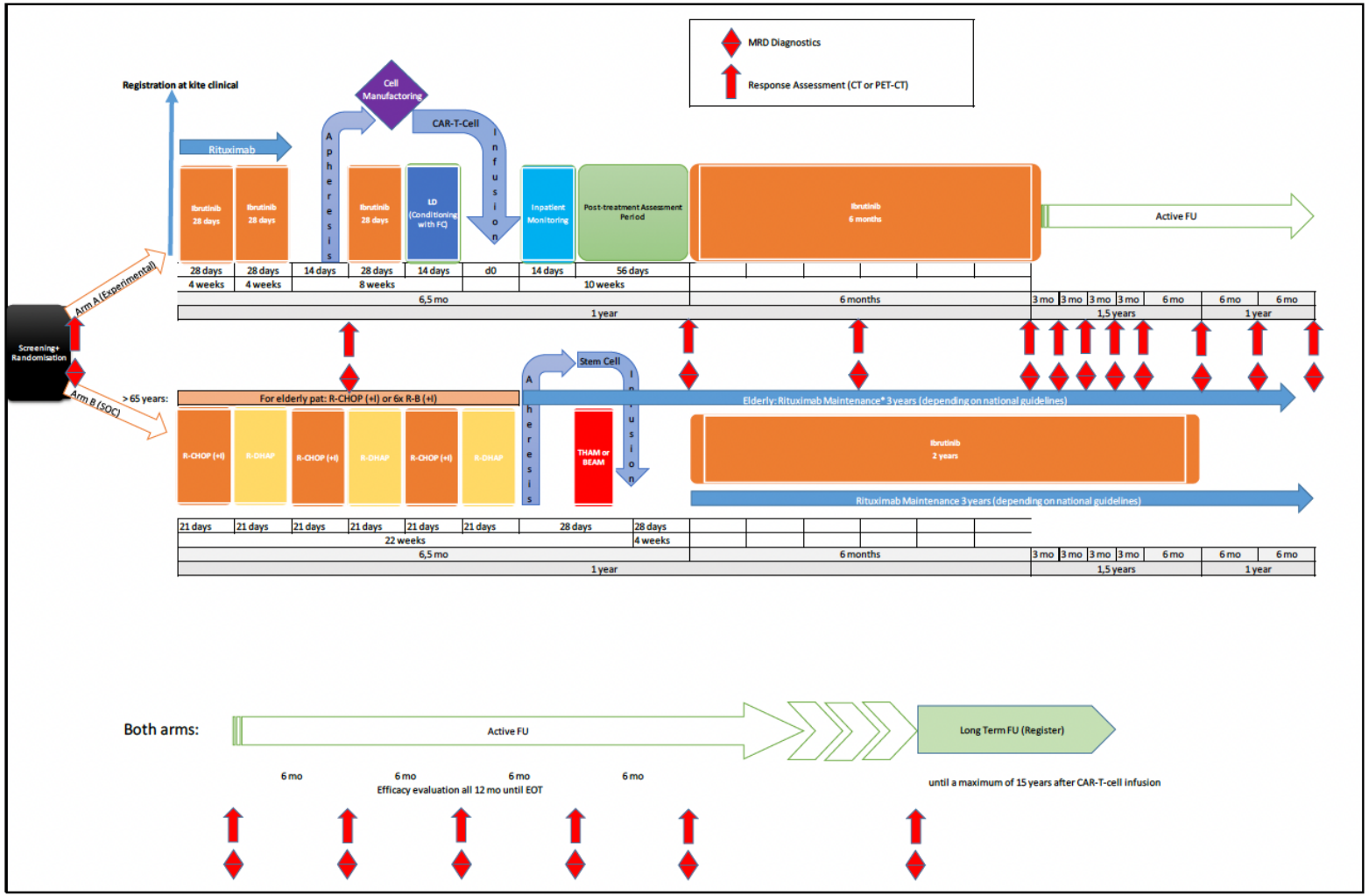


A arm: R-CHOP/R-DHAP+ASCT; A+I arm: IR-CHOP/R-DHAP+ASCT+I

Today age still dominates treatment recommendation



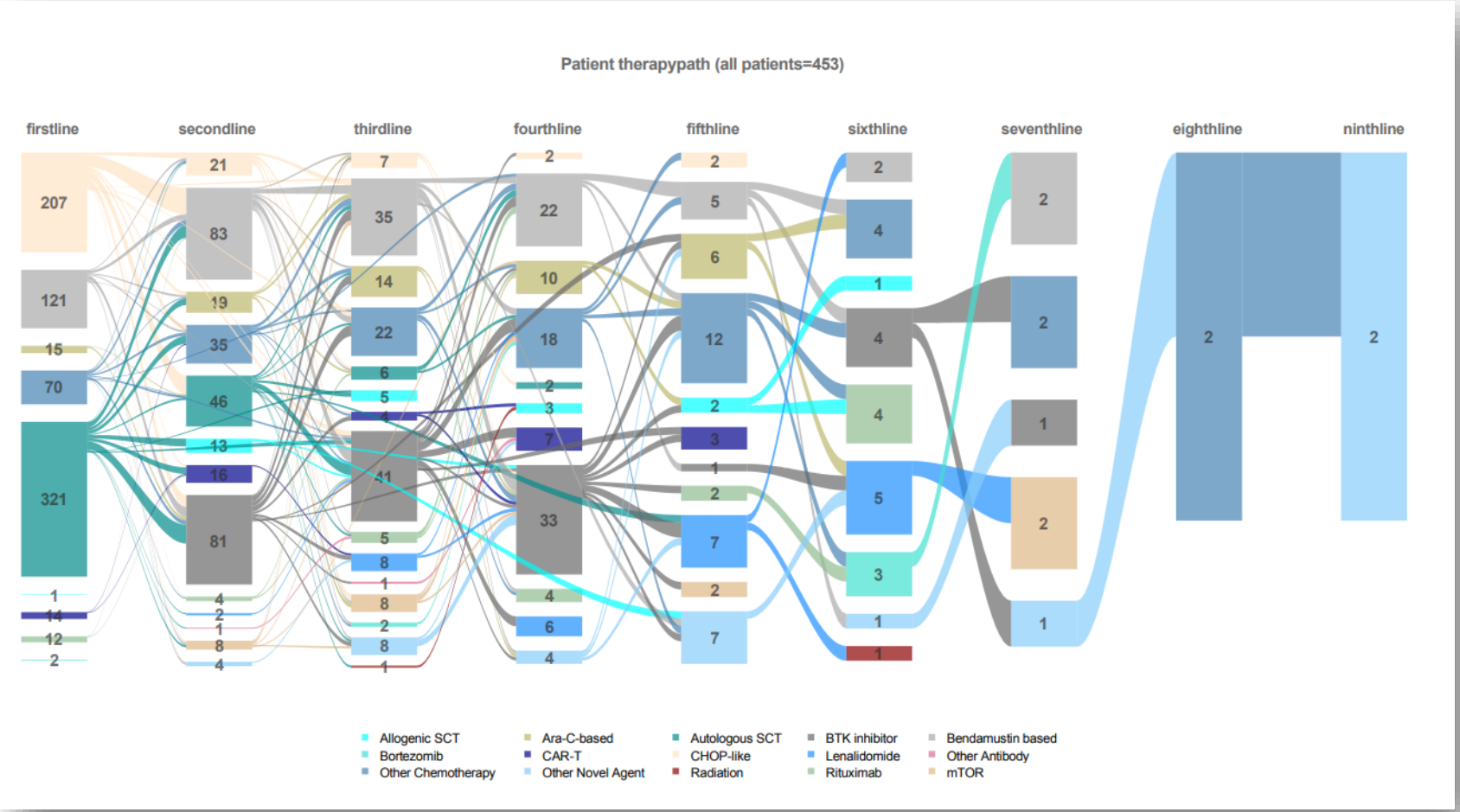
EMCL-Trial strategy for HighRisk CAR-T in firstline



Summary

- Mantle Cell Lymphoma prognosis has improved over the recent years
  - Introducion of ARA-C, Rm and in the past HDT
  - Introduction of BTK in relapse and now firstline, at least for younger patients
- High risk definition
  - Still can not be used for treatment recommendation in every patient
  - In younger: TRIANGLE like treatment would be the primary choice
  - In elderly patients optimal treatment yet to be defined
    - Waiting especially for results of ENRICH, OASIS, VIRAL
  - Incorporation of new approaches (CAR‘s, Bispecs etc) highly attractive.

Understand treatment pathways



EUROPEAN mcl NETWORK

> 1500 patients included
10 countries open
Open for cooperation / collaboration
→ www.emcl-register.net

Thank you | Discussion