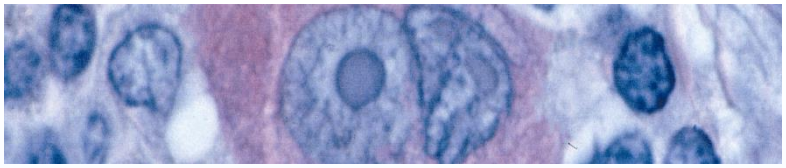


internet: www.lymphome.de • email: lymphome@medizin.uni-koeln.de

*Symposium des KML * DGHO 2019 * Berlin, 14. Oktober 2019*

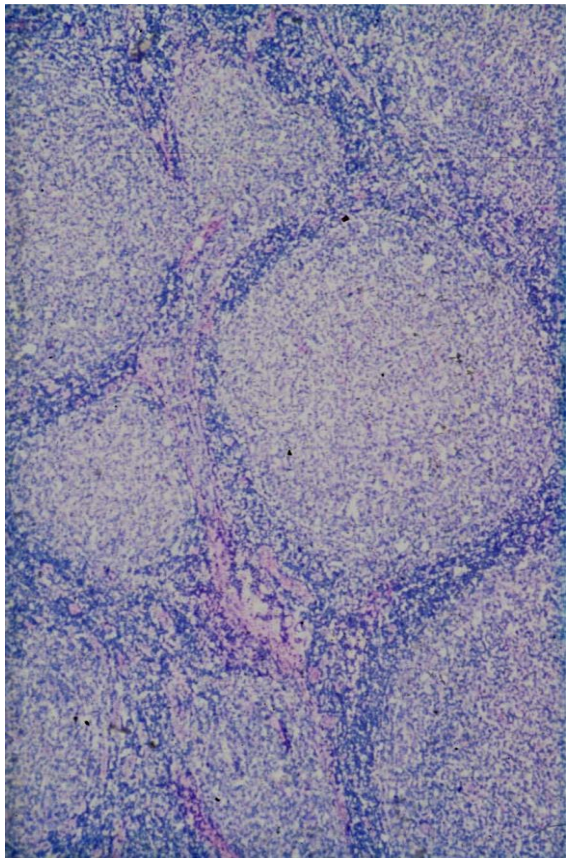
Speed-Report:

Indolente Lymphome

Prof. Dr. M. Dreyling
Med. Klinik III
Klinikum Grosshadern
LMU/München

Follicular lymphoma:

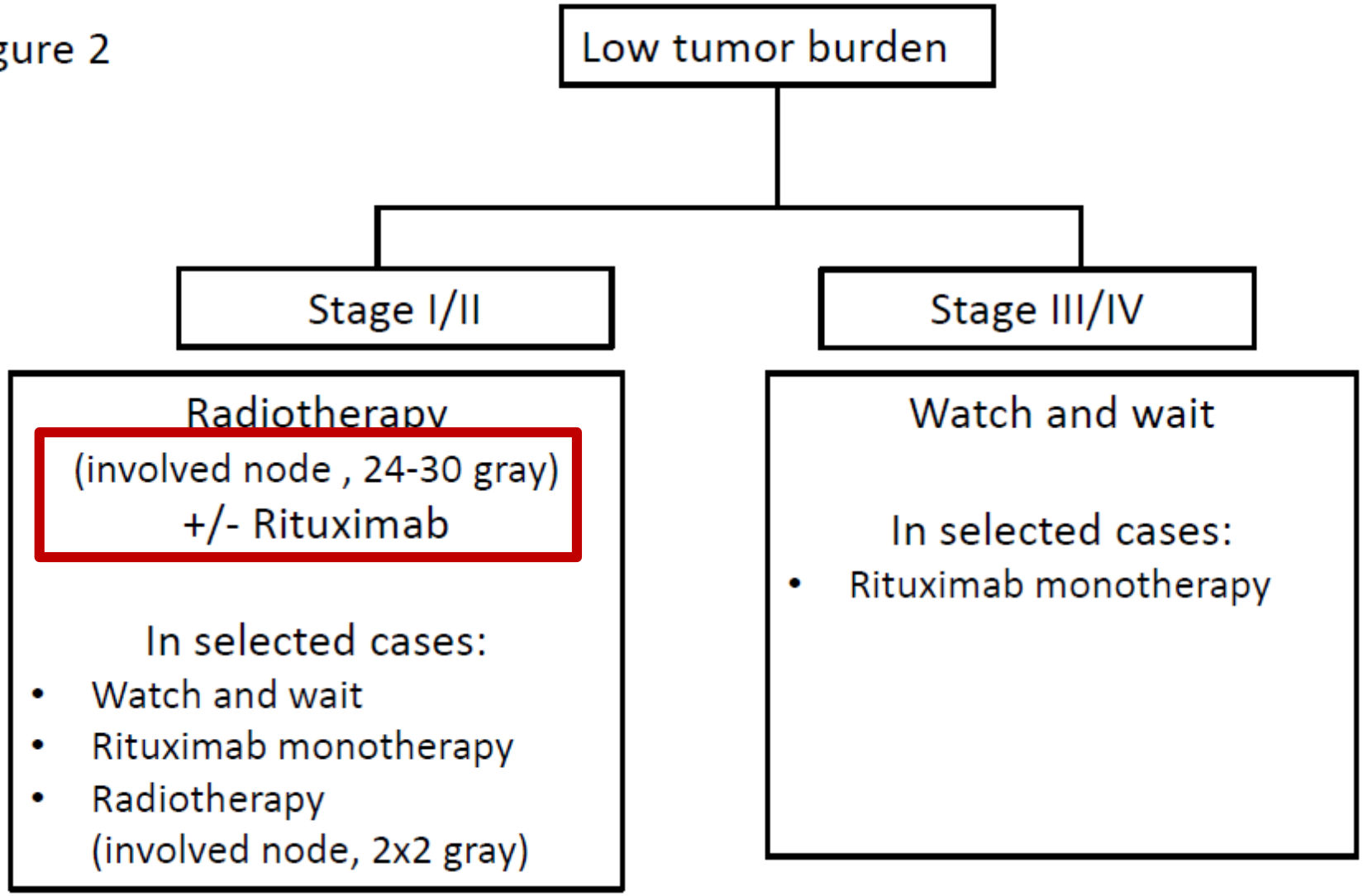
Clinical characteristics



- about 25% of lymphoma
- Median age 60-65 years
- 85% advanced stage III/IV
- Indolent clinical course (median survival 15-20 years)
- In relapse still sensitive to therapy

FOLLICULAR LYMPHOMA
ESMO/EHA THERAPEUTIC ALGORITHM 2020

Figure 2



Follicular Lymphoma

Stadium I/II: Radiatio + Rituximab (n=85)

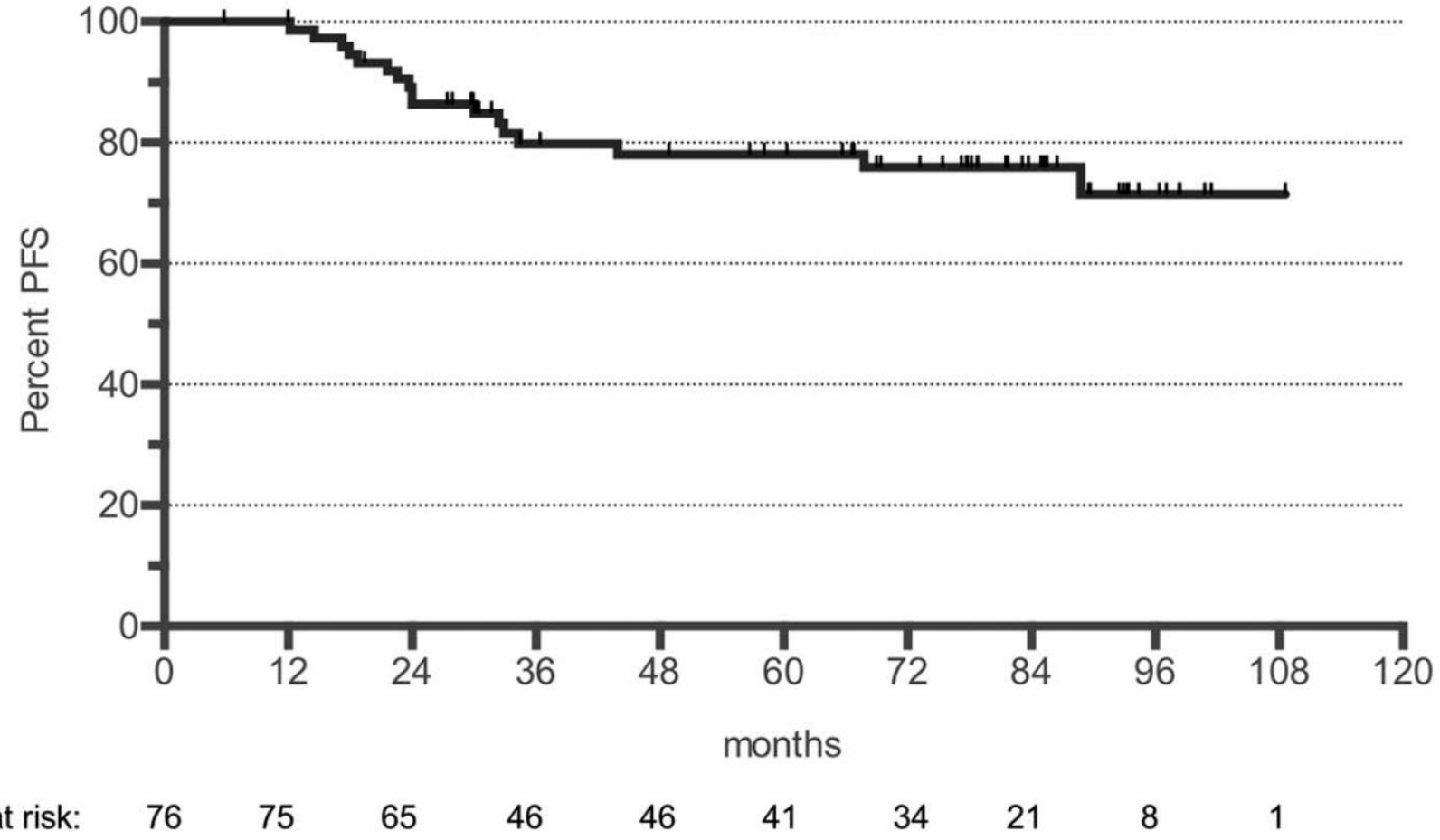
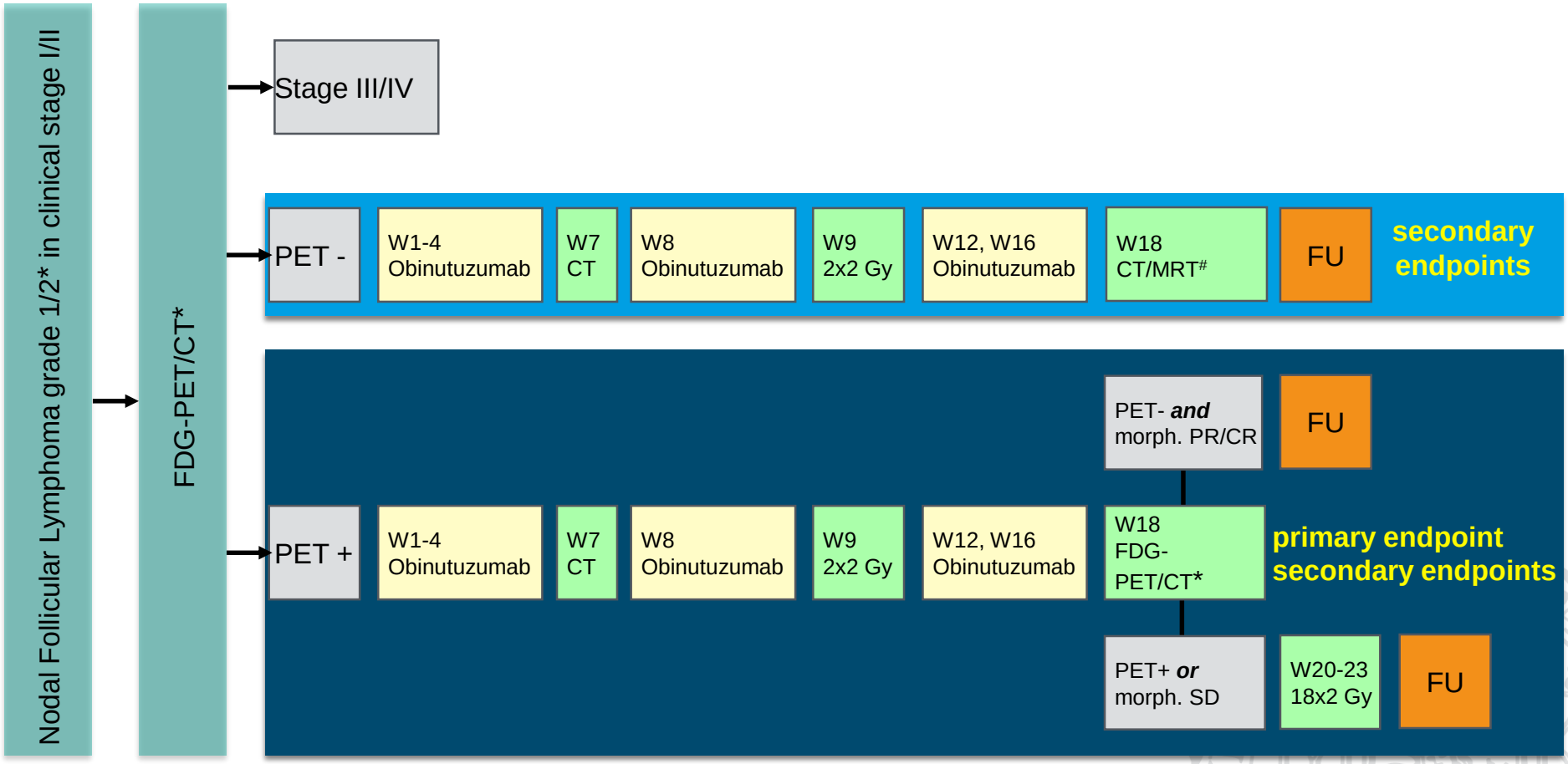


Figure 1. **PFS of the PP set (median follow-up 66 months)**. PFS = progression-free survival, PP = per protocol.

Herfarth, Hemasphere 2018

GAZAI

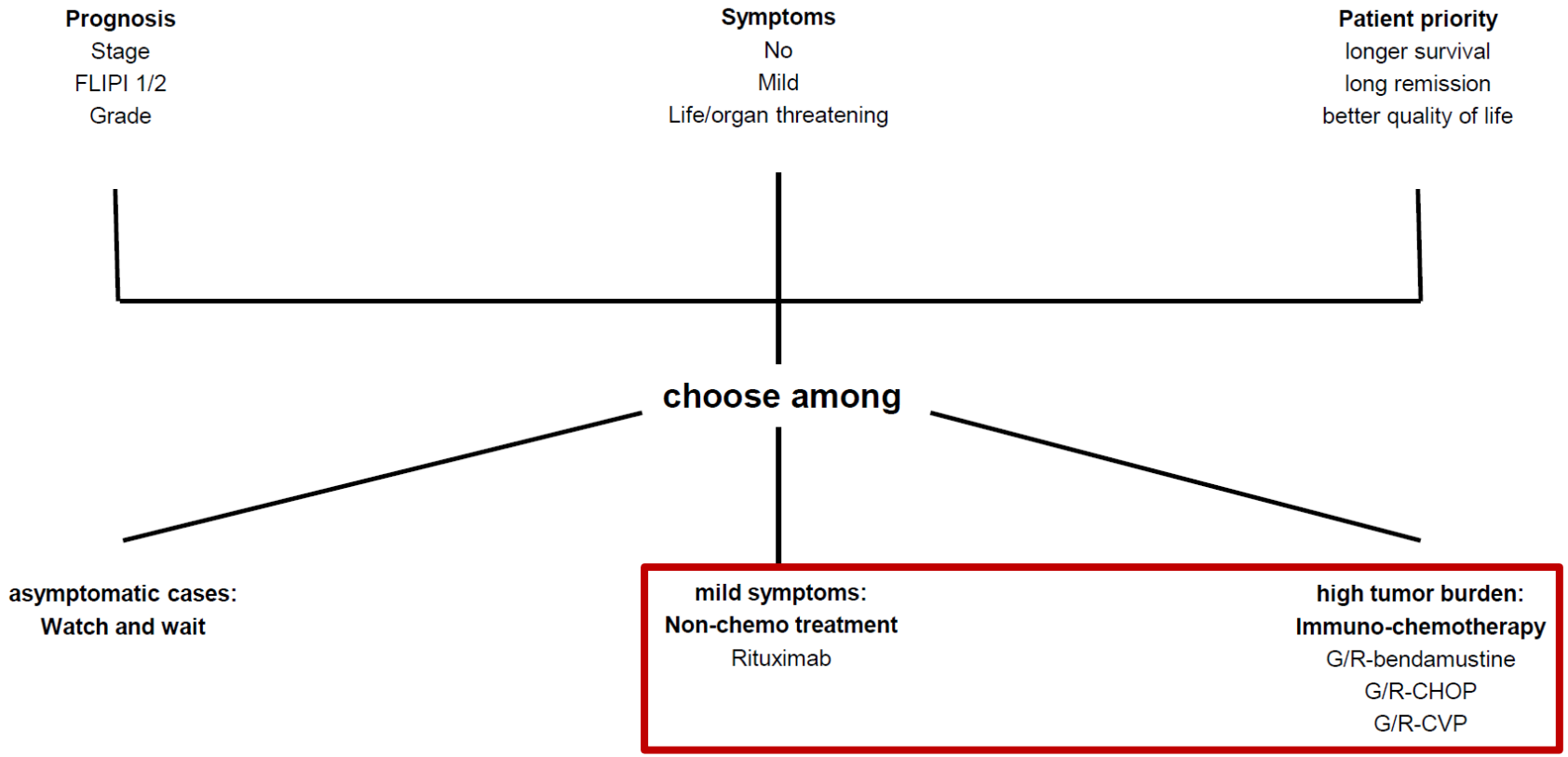
Multi Center Phase 2 Study
max. 93 patients



= only in case of initially enlarged PET negative lymph nodes

* = centrally reviewed

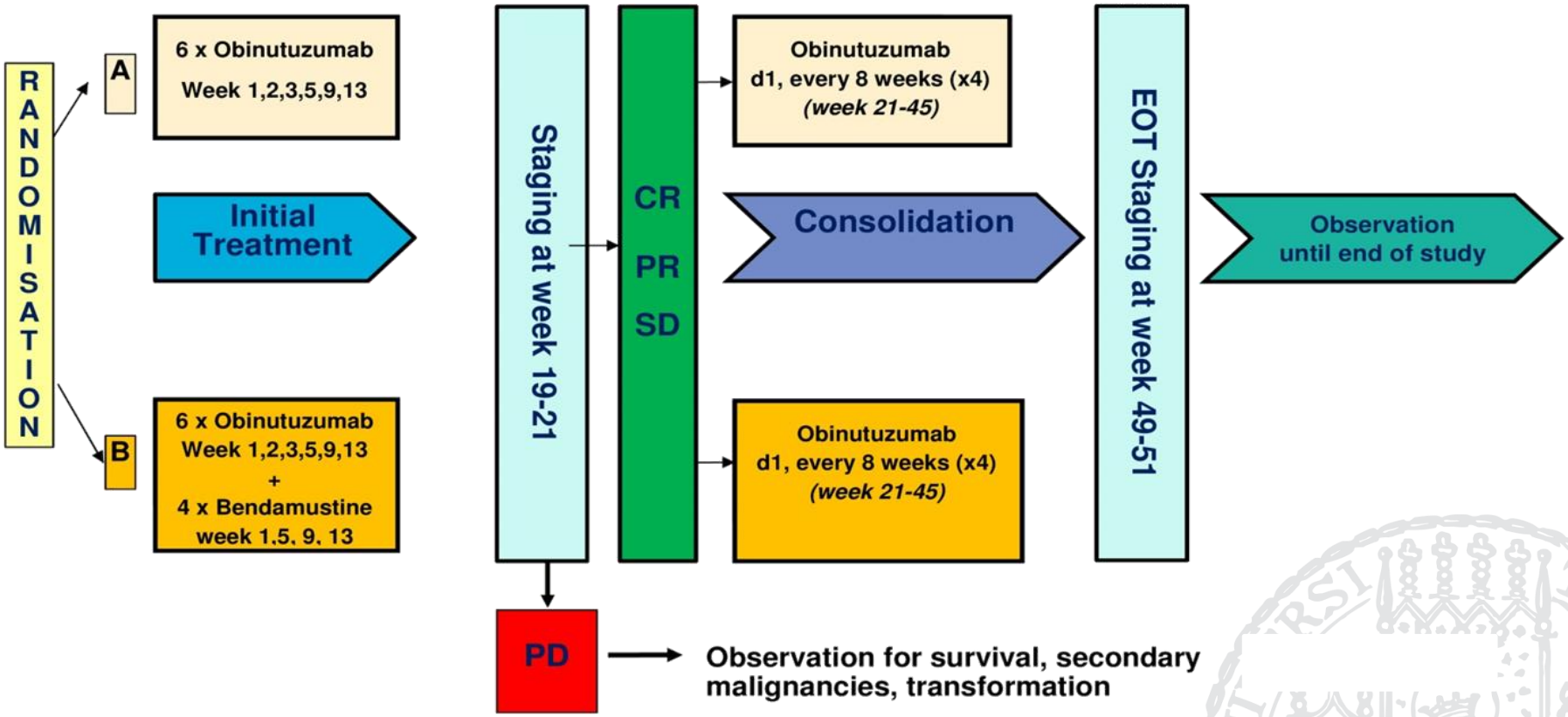
FOLLICULAR LYMPHOMA
ESMO/EHA THERAPEUTIC ALGORITHM 2020



consider
Antibody maintenance
(or radioimmunotherapy)

Rituximab/lenalidomide
In selected patients
(off label)

GABE STUDIE


RANDOMISATION
A
6 x Obinutuzumab
Week 1,2,3,5,9,13
Initial Treatment
B
6 x Obinutuzumab
Week 1,2,3,5,9,13
+
4 x Bendamustine
week 1,5, 9, 13
Staging at week 19-21
CR
PR
SD
PD
Obinutuzumab
d1, every 8 weeks (x4)
(week 21-45)
Consolidation
Obinutuzumab
d1, every 8 weeks (x4)
(week 21-45)
EOT Staging at week 49-51
Observation
until end of study
Observation for survival, secondary
malignancies, transformation

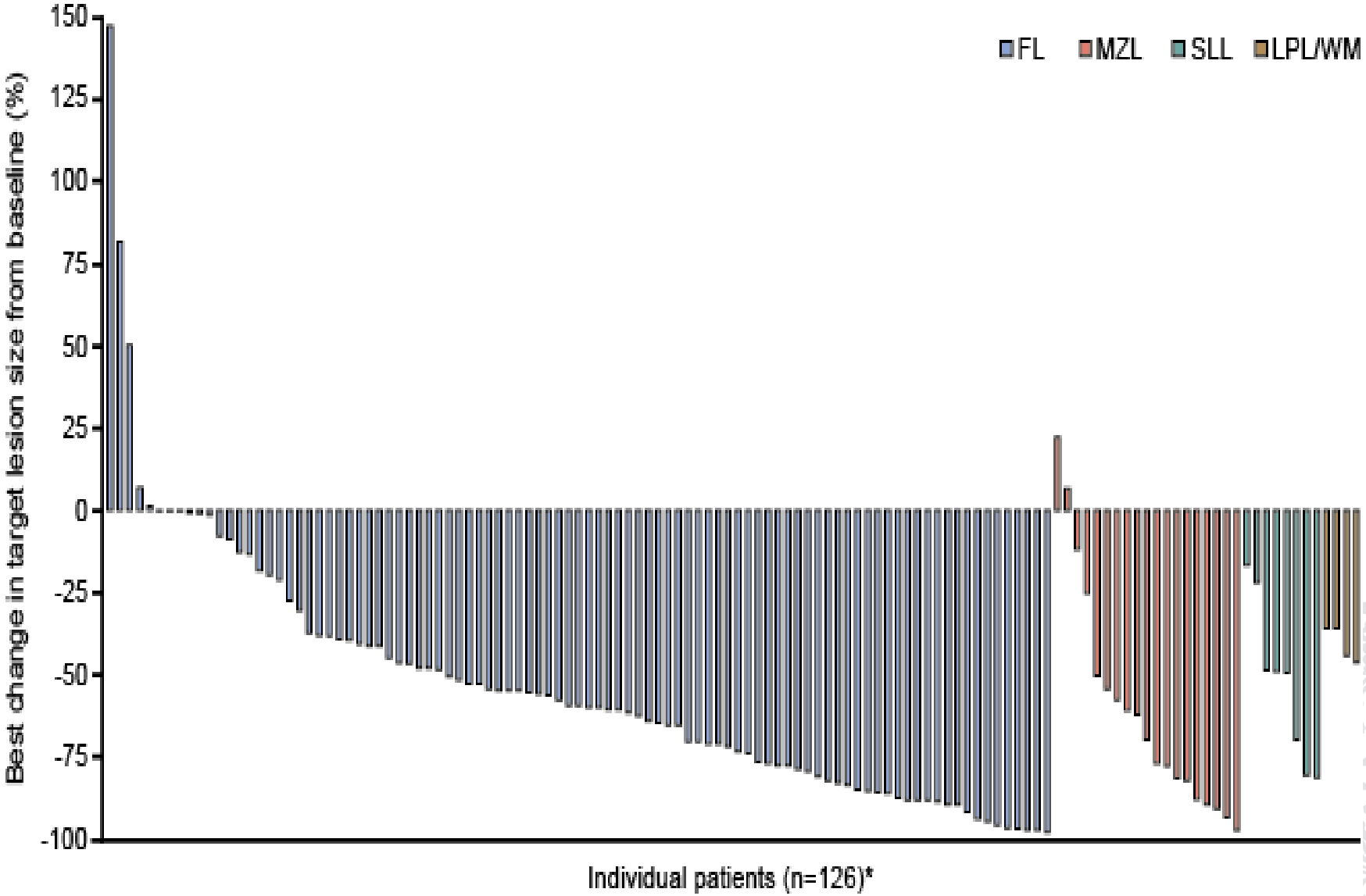
Follicular Lymphoma

EHA/ESMO therapeutic algorithm 2020

<65 years +	>65 years +
Immunochemotherapy (BG/R, G/R-CHOP, G/R-CVP) CR/PR: Discuss antibody maintenance In selected cases: • Rituximab monotherapy • Rituximab-lenalidomide*	Immunochemotherapy (BG/R, G/R-CHOP, G/R-CVP) CR/PR: Discuss antibody maintenance In selected cases: • Rituximab monotherapy • Rituximab-lenalidomide*
First Relapse/progression	
Immunochemotherapy# CR/PR: Discuss antibody maintenance In selected cases: • Rituximab monotherapy • ASCT (early relapses, transformation) • Rituximab-lenalidomide* (early relapses)	Immunochemotherapy# CR/PR: Discuss antibody maintenance In selected cases: • Rituximab monotherapy • Radioimmunotherapy • Rituximab-lenalidomide* (early relapses)
Later Relapse/progression	
• Immunochemotherapy# (long prior remissions) • Rituximab monotherapy • Rituximab-lenalidomide* In selected cases: • ASCT (early relapses, transformation) • Radioimmunotherapy • Idelalisib (double refractory) • allogeneic transplantation	• Immunochemotherapy# (long prior remissions) • Rituximab monotherapy • Rituximab-lenalidomide* In selected cases: • Radioimmunotherapy • Idelalisib (double refractory)

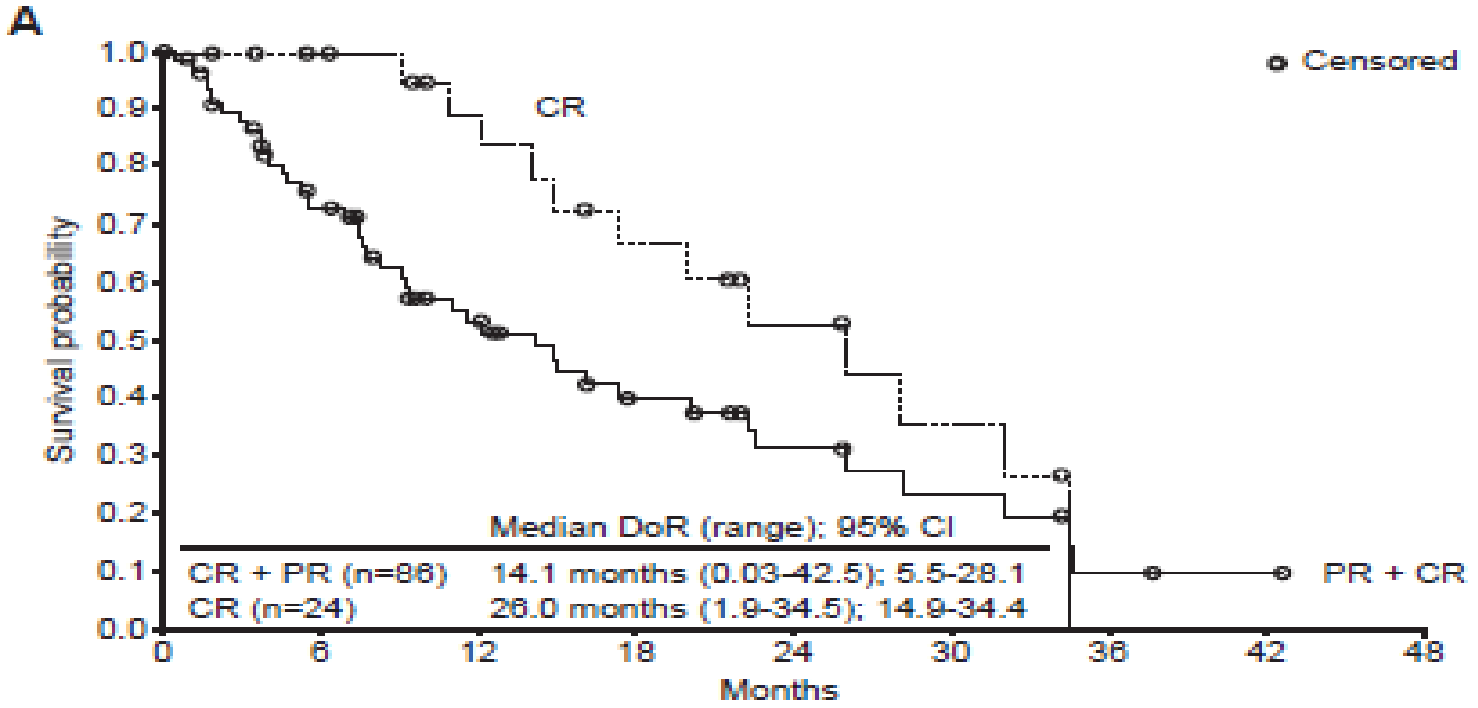
+ biological age; *off label ; # G preferred in R-refractory cases

Copanlisib in relapsed indolent lymphoma



Dreyling, submitted 2019

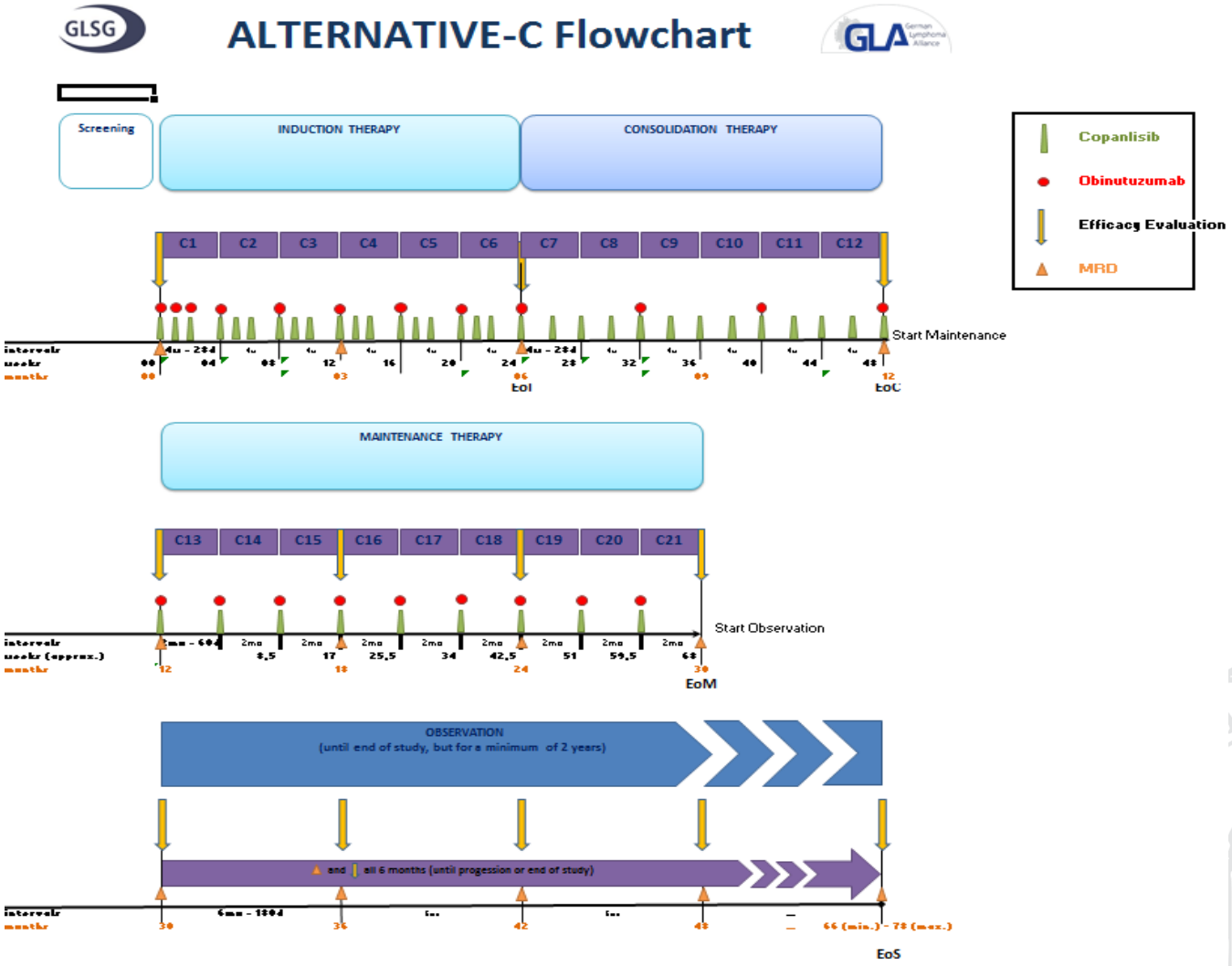
Copanlisib in relapsed indolent lymphoma



Number of patients at risk

PR + CR	86	51	31	22	16	10	6	5	1	0
CR	24	22	19	14	11	7	4	3	0	

ALTERNATIVE-Copanlisib



Follicular lymphoma

GLSG Studies 2018

Alternative 1:
G-Ibru
↓
G-Ibru maintenance

Alternative 2:
G-Copanilisib
↓
G-Copanlisib maintenance

medically non-fit:
G +/- Bendamustine
↓
G maintenance

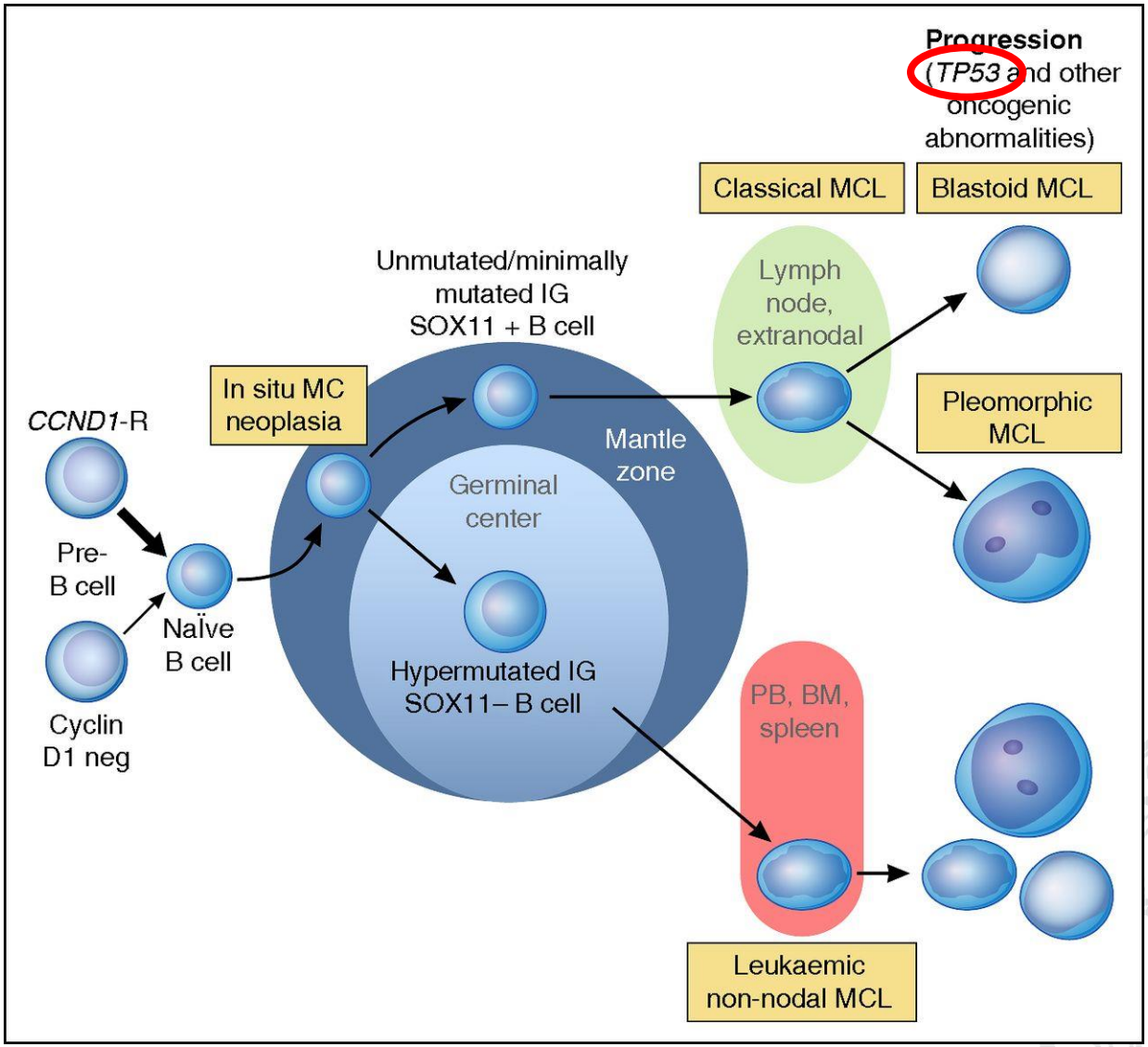
Relapse

FLAZ:
ASCT vs. RIT

BeRT:
R-BendaTemsirolimus

ReBeL:
R2 +/- Benda
↓
R-maintenance

MCL: *two kind of diseases*



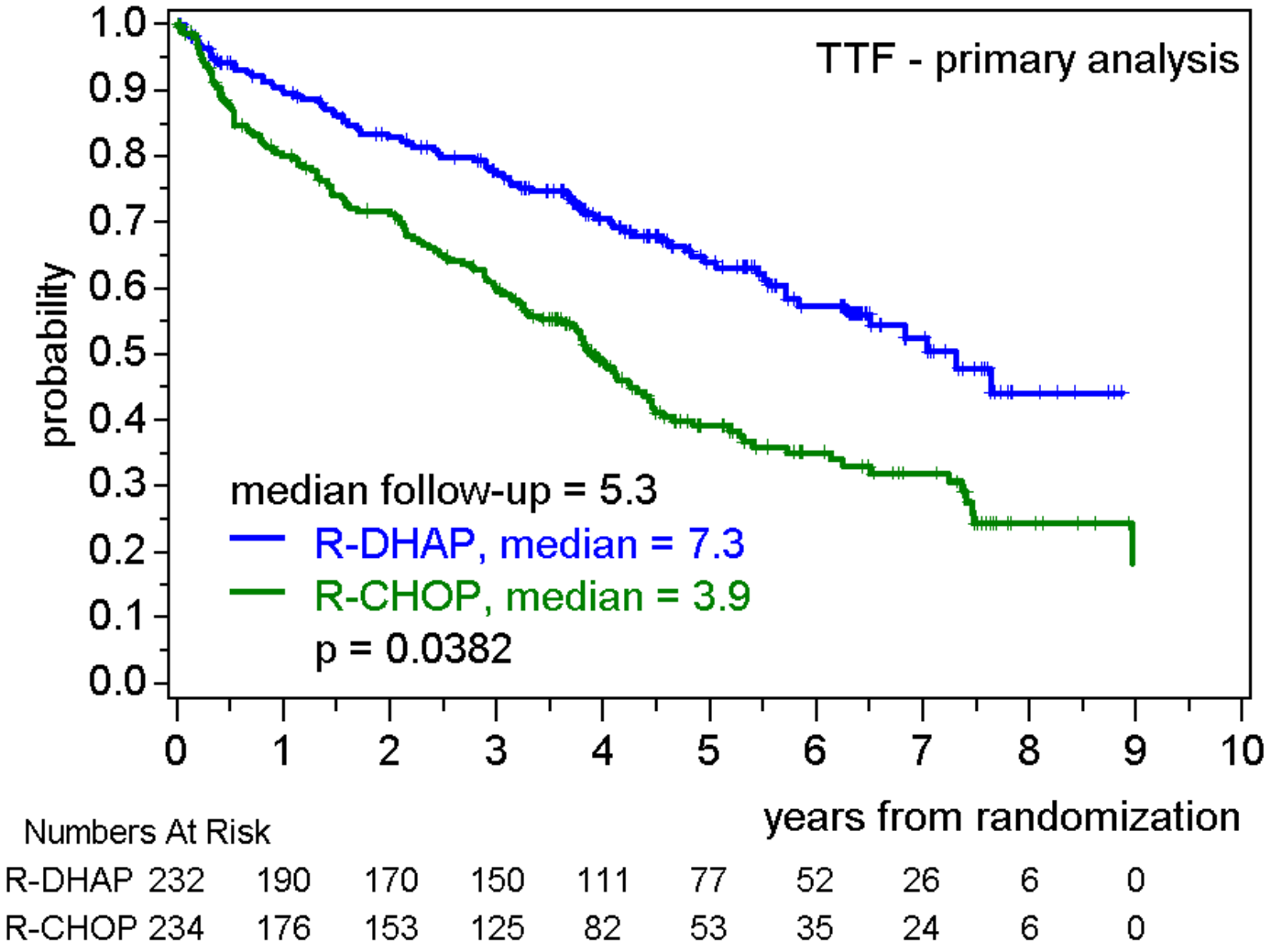
Dreyling, ESMO CR 2017

young patient (≤65)	elderly patient (>65)	compromised patient
First line treatment		
dose-intensified immuno-chemotherapy (e.g. R-CHOP, high dose Ara-C) ⇒ Autologous SCT ⇒ Rituximab maintenance	conventional immuno-chemotherapy (e.g. R-CHOP, VR-CAP, BR, R-BAC) ↓ Rituximab maintenance	Best supportive care? R-Chlorambucil BR (dose-reduced) R-CVP
1. relapse		
immuno-chemotherapy (e.g. R-BAC, BR) or targeted approaches ↓ discuss: - allogeneic SCT	immuno-chemotherapy (e.g. BR, R-BAC) or targeted approaches ↓ discuss: - Rituximab maintenance - radioimmunotherapy	Immuno-chemotherapy (e.g. 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

MCL younger

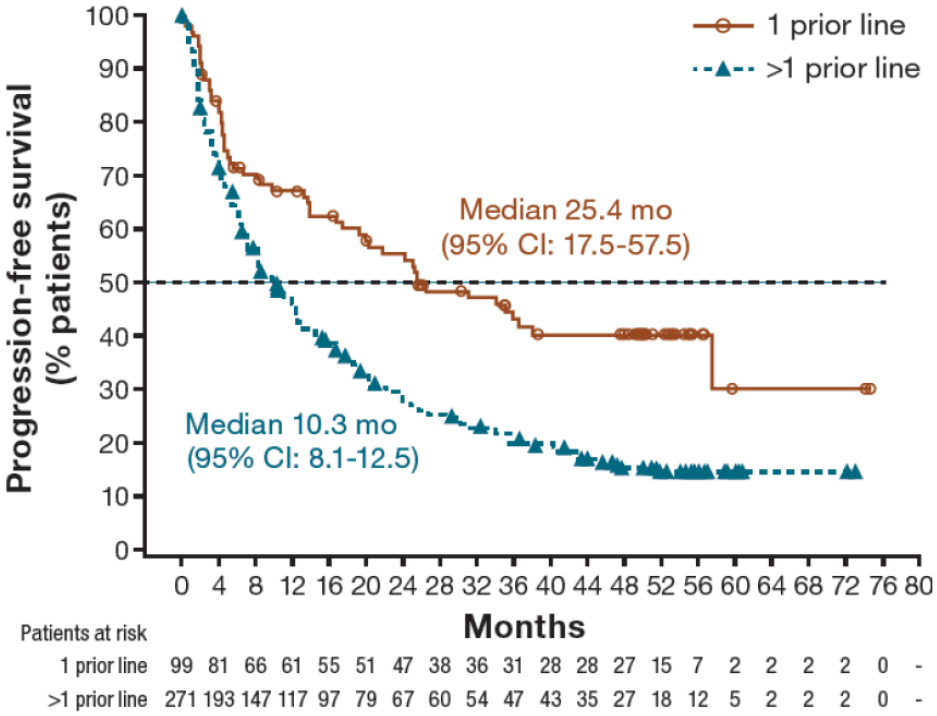
Time to treatment failure

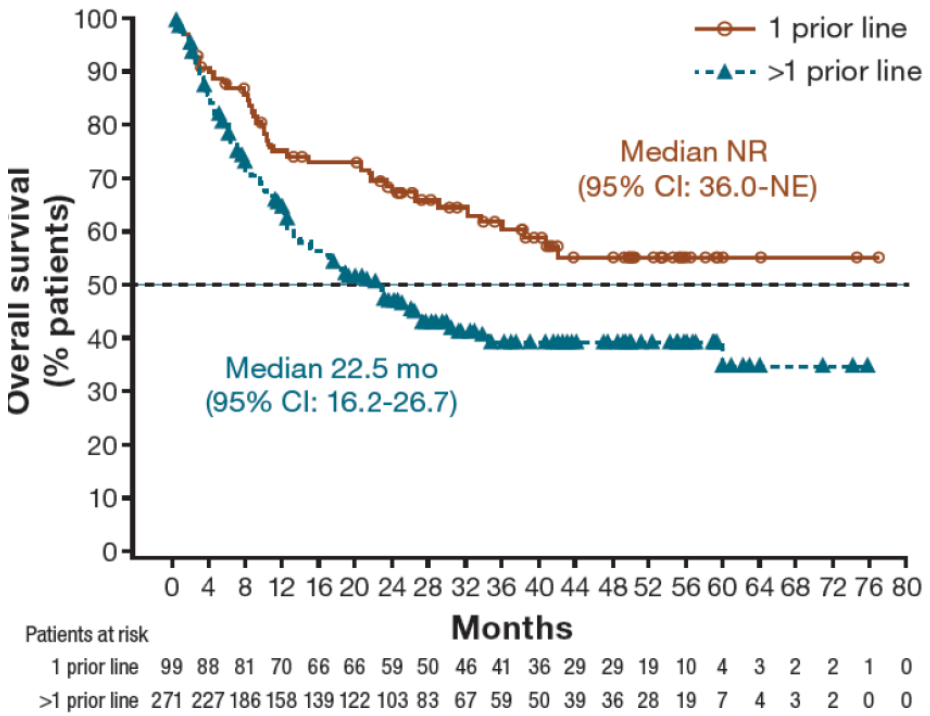


Hermine, Lancet 2016

Pooled study analysis

Survival rates

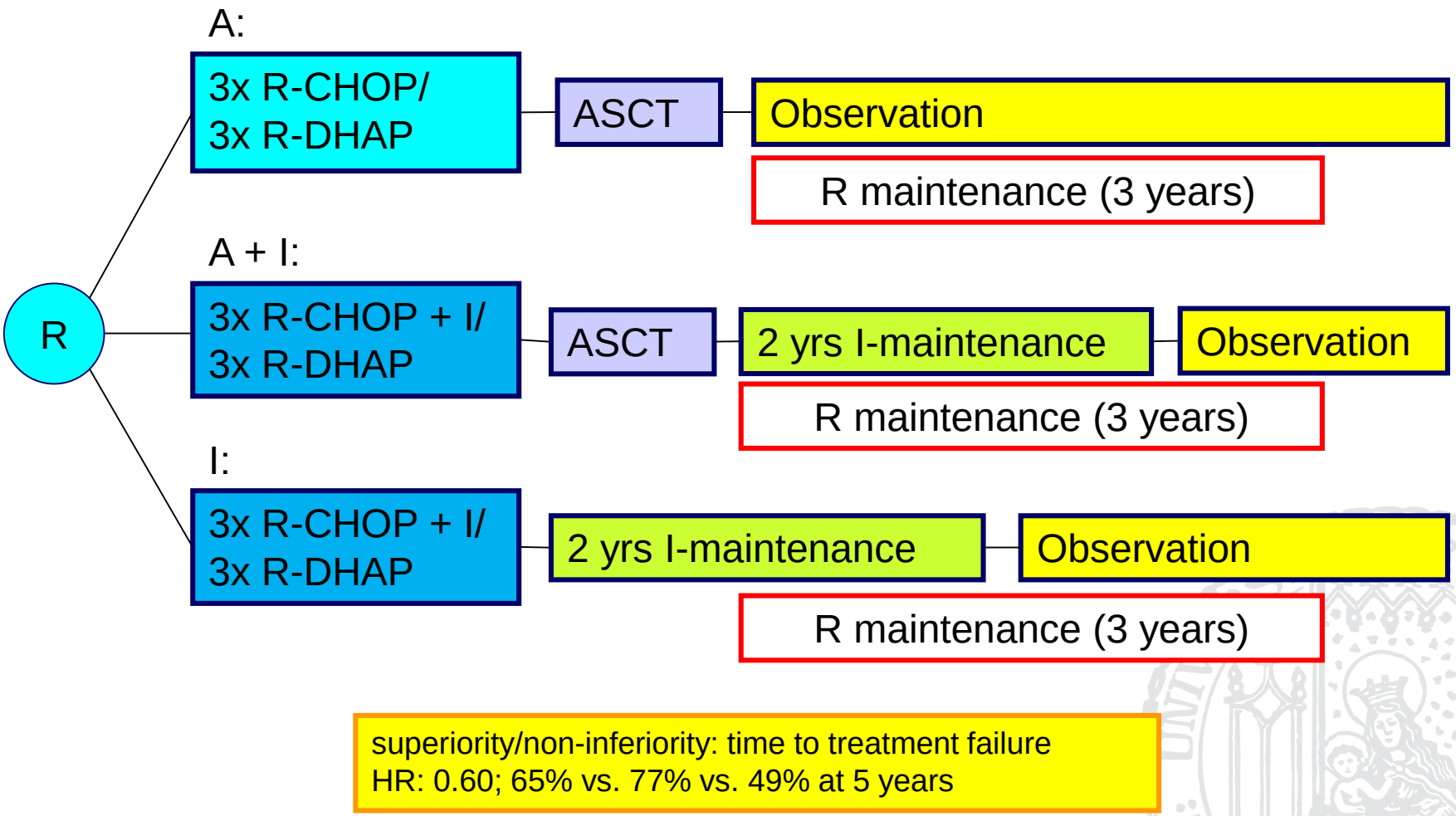




Rule, Haematologica 2018

TRIANGLE

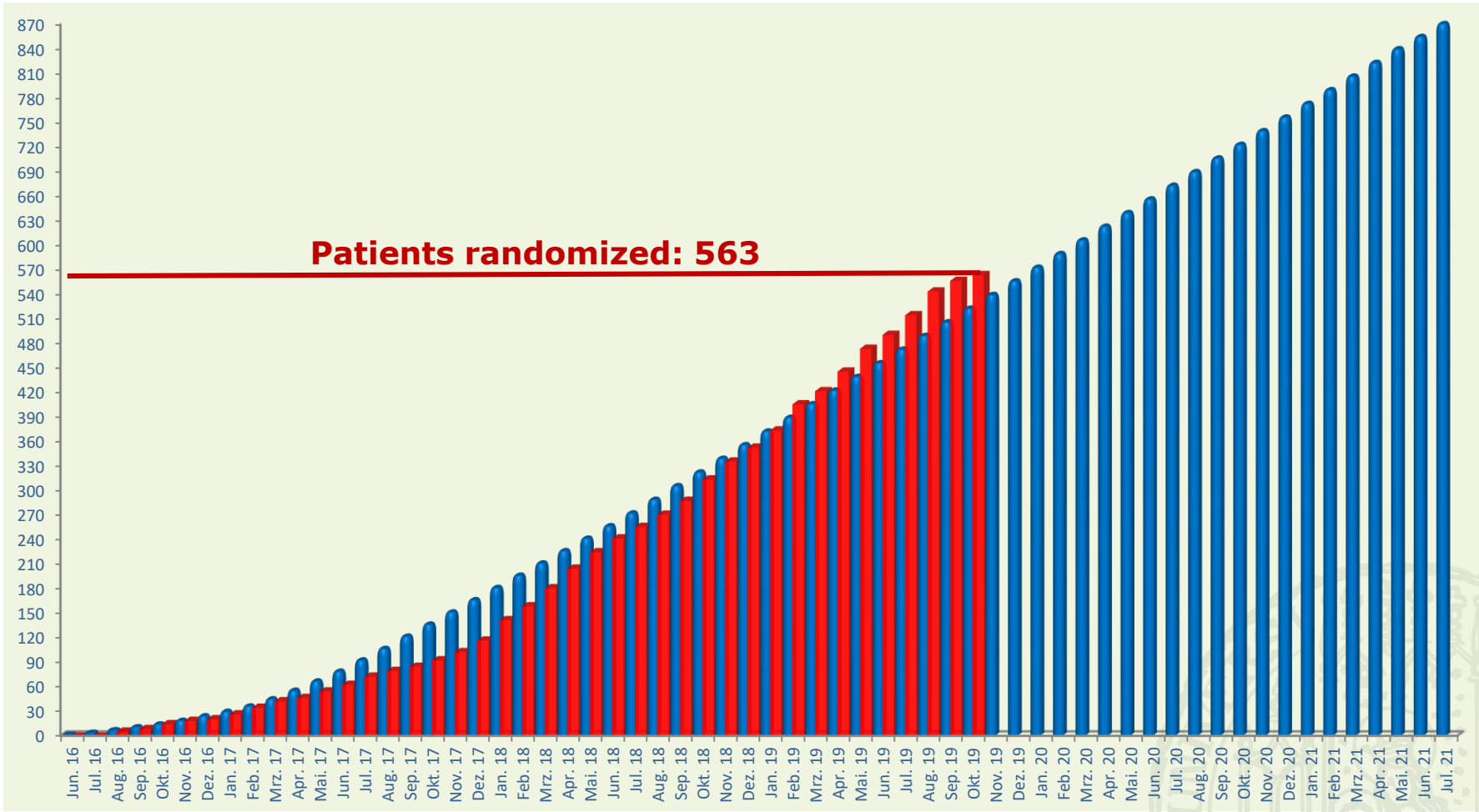
ADD ON VS HEAD TO HEAD COMPARISON



superiority/non-inferiority: time to treatment failure
HR: 0.60; 65% vs. 77% vs. 49% at 5 years

European MCL Network

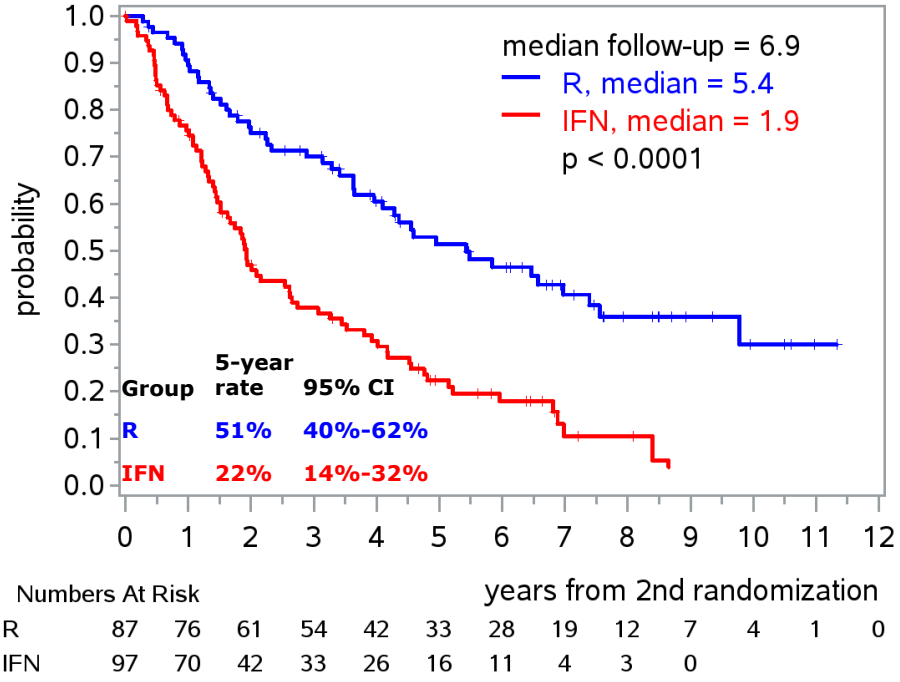
MCL younger 2: Triangle



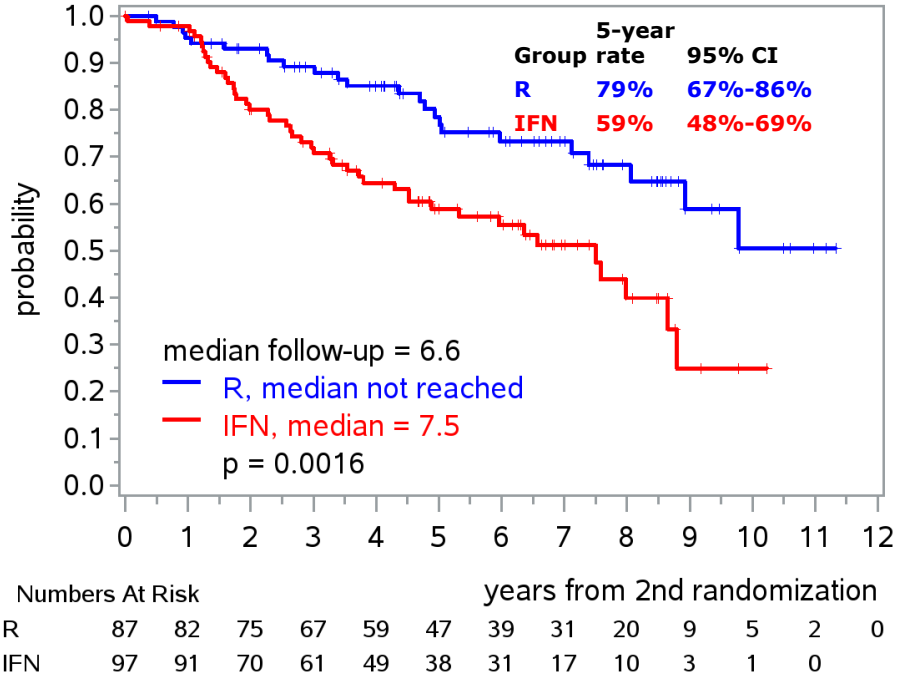
MCL elderly
R-CHOP +/- R maintenance

Updated results 2017: Maintenance part (R2) – after R-CHOP

PFS



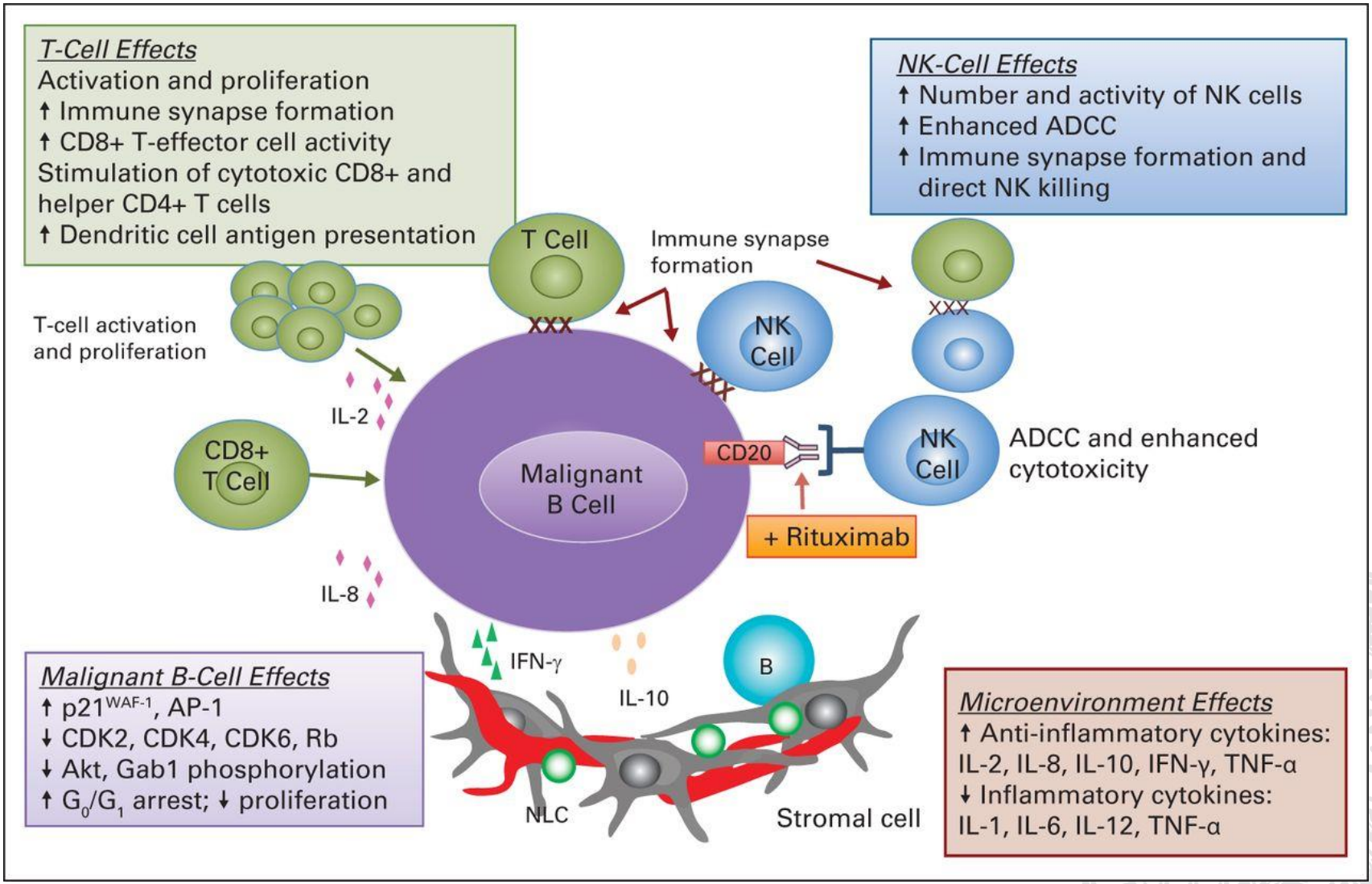
OS



Kluin-Nelemans, JCO 2019

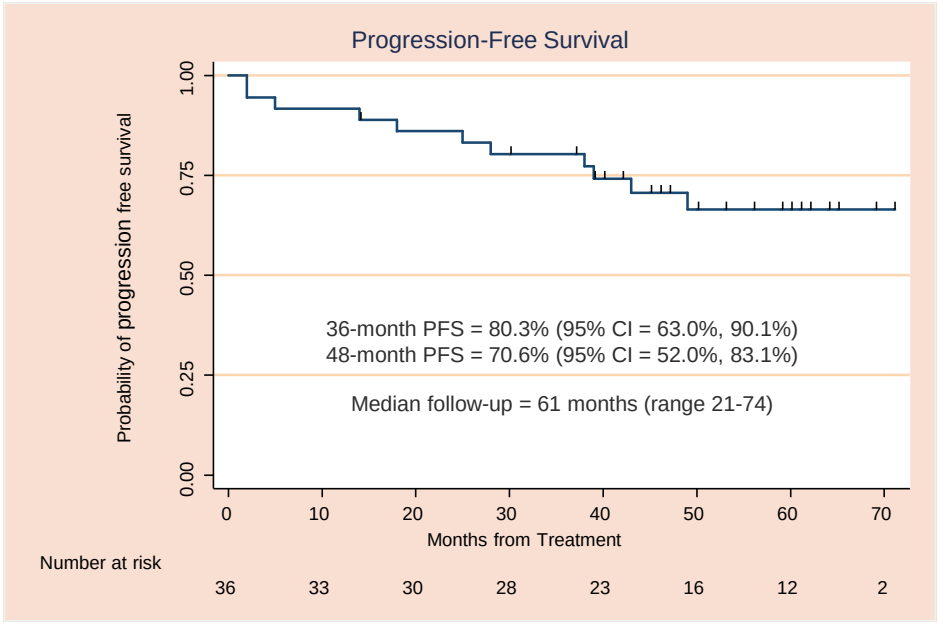
Lenalidomide

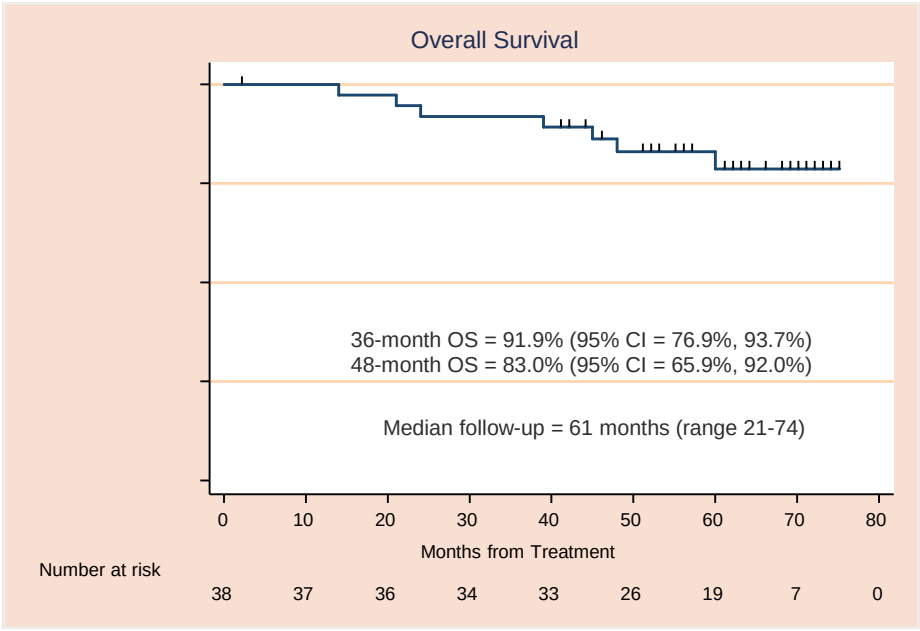
Mechanisms of action



Gribben, JCO 2015

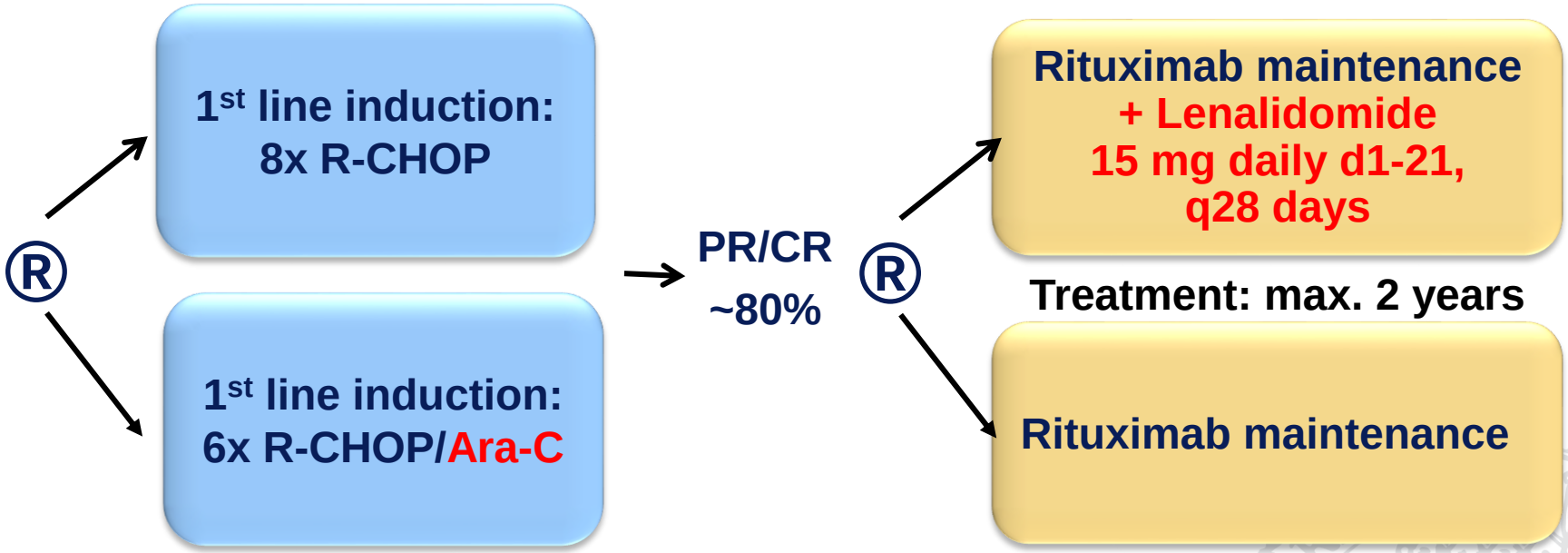
Survival


Progression-Free Survival
Probability of progression free survival
1.00
0.75
0.50
0.25
0.00
36-month PFS = 80.3% (95% CI = 63.0%, 90.1%)
48-month PFS = 70.6% (95% CI = 52.0%, 83.1%)
Median follow-up = 61 months (range 21-74)
0
10
20
30
40
50
60
70
Months from Treatment
Number at risk
36
33
30
28
23
16
12
2


Overall Survival
36-month OS = 91.9% (95% CI = 76.9%, 93.7%)
48-month OS = 83.0% (95% CI = 65.9%, 92.0%)
Median follow-up = 61 months (range 21-74)
0
10
20
30
40
50
60
70
80
Months from Treatment
Number at risk
38
37
36
34
33
26
19
7
0

European MCL Network

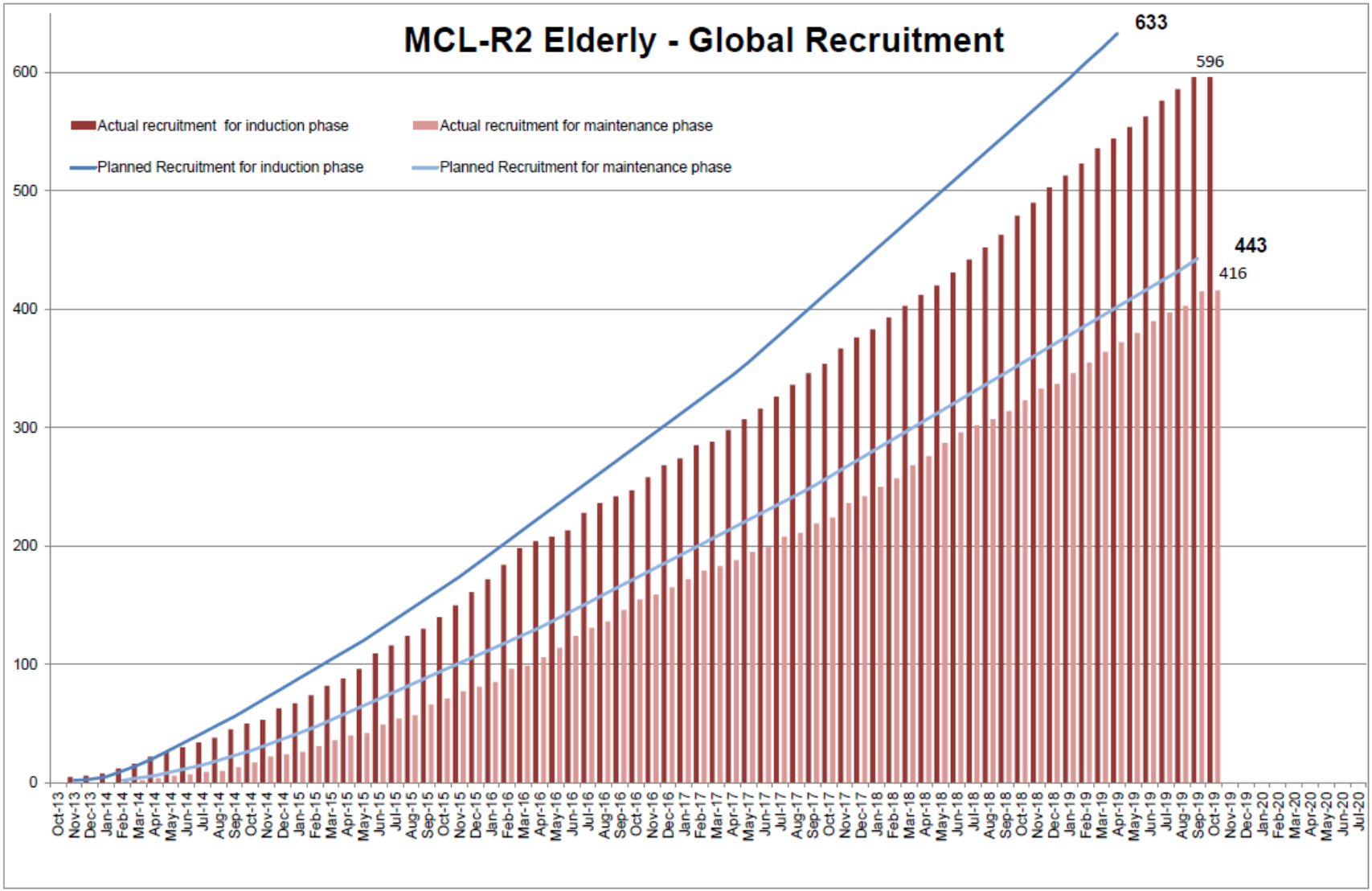
MCL R2 elderly



sponsor: LYSARC
central pathology: W. Klapper
MRD diagnostics: M. Ladetto, C. Pott, MH Delfau

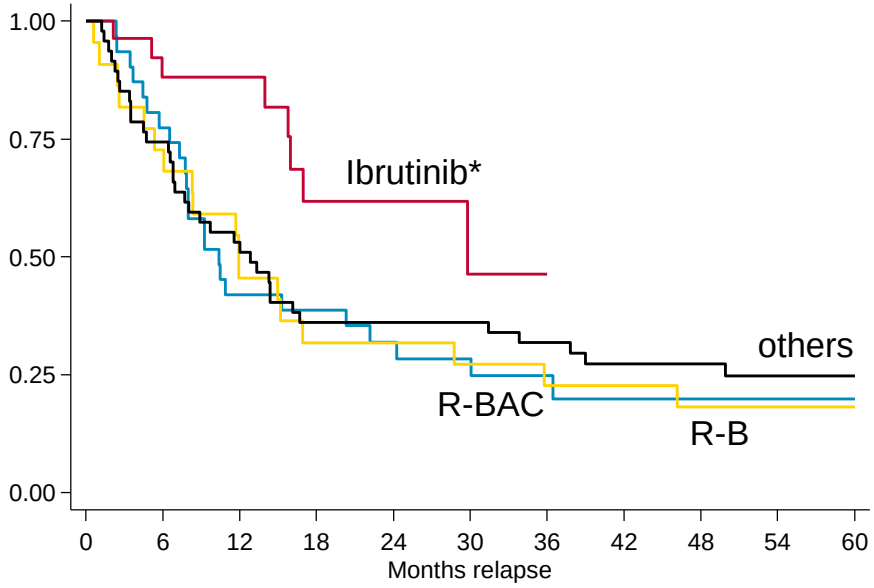
European MCL Network

MCL R2 elderly



OS, early versus late POD

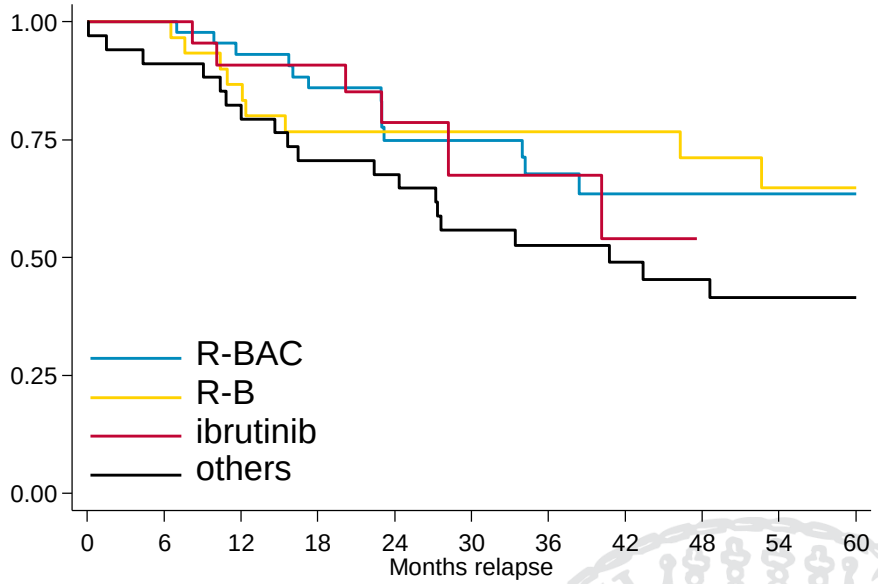
Early POD



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

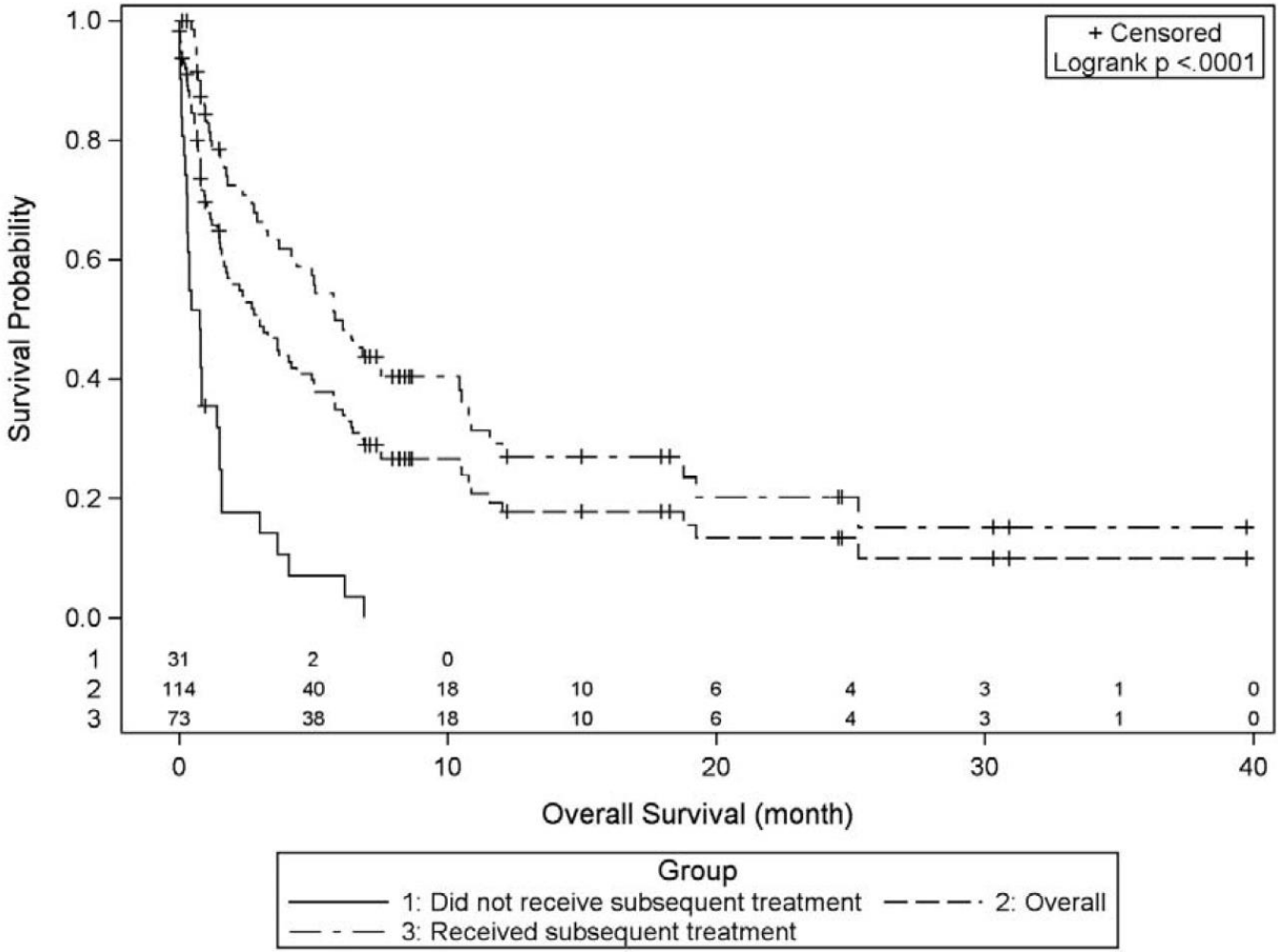


At risk:											
BAC	45	45	40	35	26	23	16	14	12	8	7
BR	32	30	26	23	22	20	16	15	13	10	9
ibru	23	22	20	18	10	6	6	4	0	0	0
other	34	31	27	24	23	19	16	13	12	8	7

Visco, ICML 2019

Relapsed mantle cell lymphoma

Failure under ibrutinib



Martin, Blood 2016

European MCL Network
Study generation 2019

< 65 years	> 60 years	> 65 years
MCL younger: **R-CHOP/DHAP =>ASCT** **R-CHOP/DHAP+I =>ASCT => I** **R-CHOP/DHAP + I => I**	***MCL elderly R2:*** **R-CHOP vs R-CHOP/Ara-C** **=> Rituximab M** **+/- Lenalidomide**	***MCL elderly I:*** **BR +/- Ibrutinib** **=> Rituximab M** **+/- Ibrutinib**

Relapse

Ibrutinib/ **Bortezomib**	**R-HAD +/- Bortezomib**	***Ibrutinib +/-*** **ABT-199**

Acknowledgements