

Interactive Debate: Aggressive Therapy In Mantle Cell Lymphoma (younger patients)

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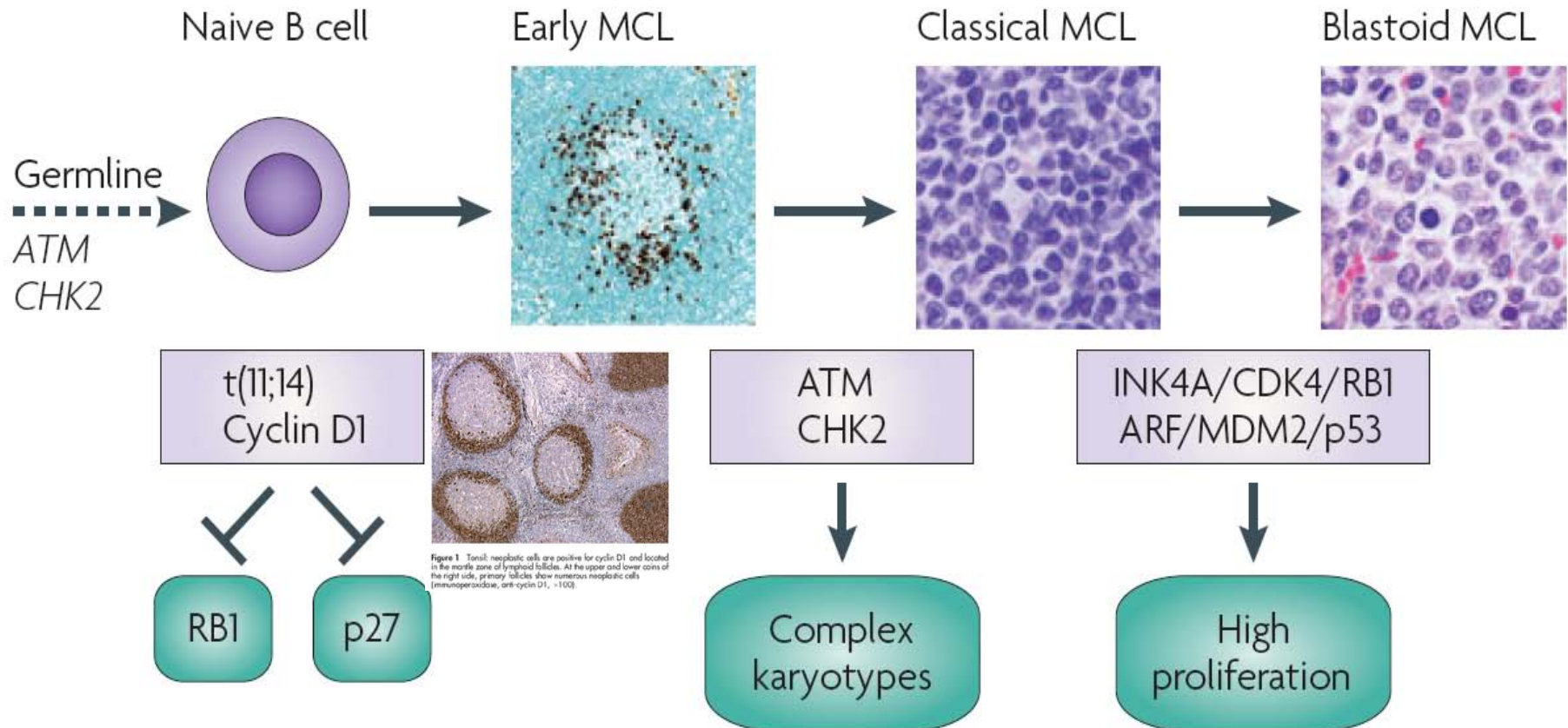


MCL: A Spectrum of Diseases

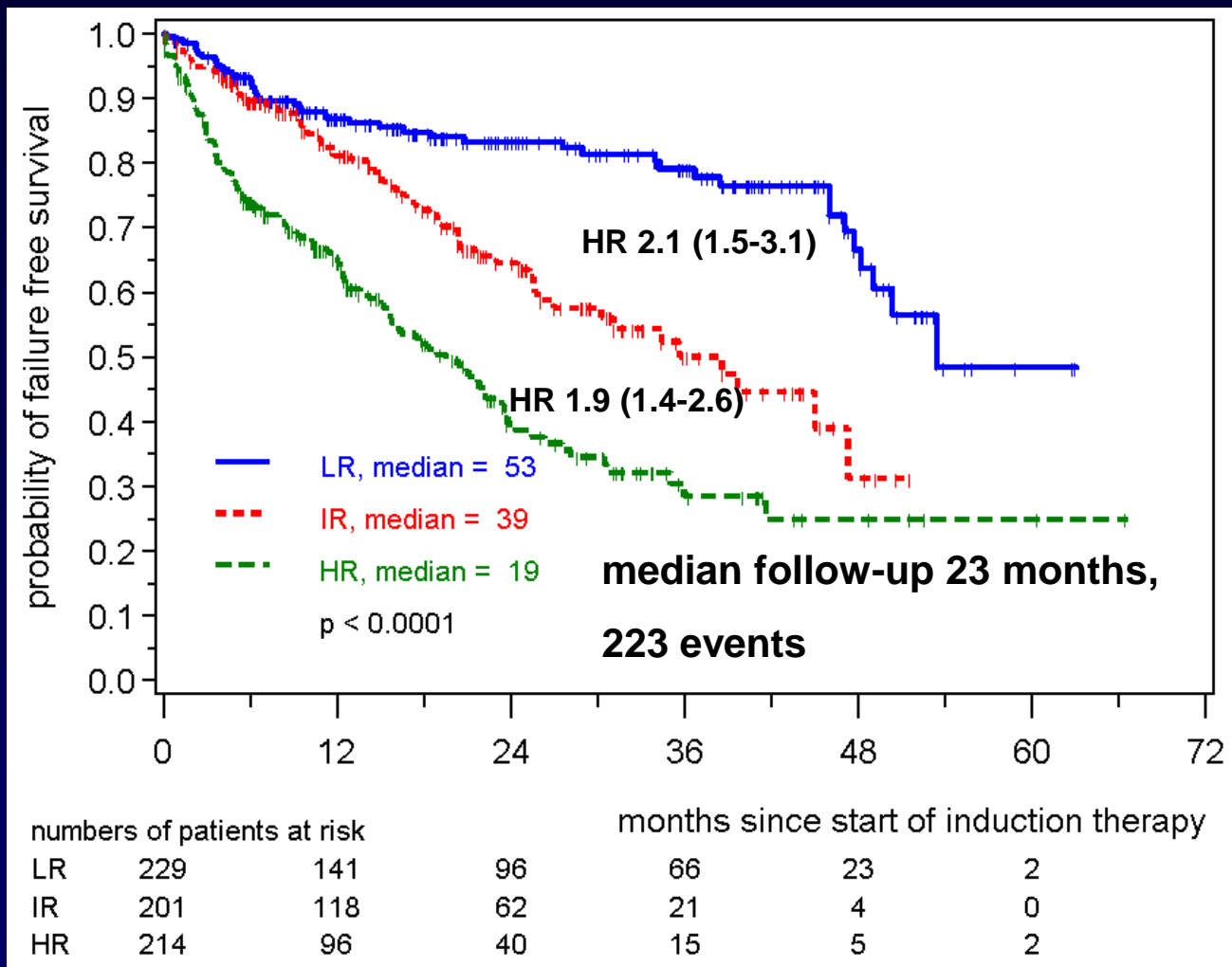
“ Indolent“ MCL (15%)

“ Classical“ MCL (80%)

“ transformed“ (5%)



Confirmation of MIPI Progression-Free Survival



(PALL: PS, age, LDH, leukocyte count)

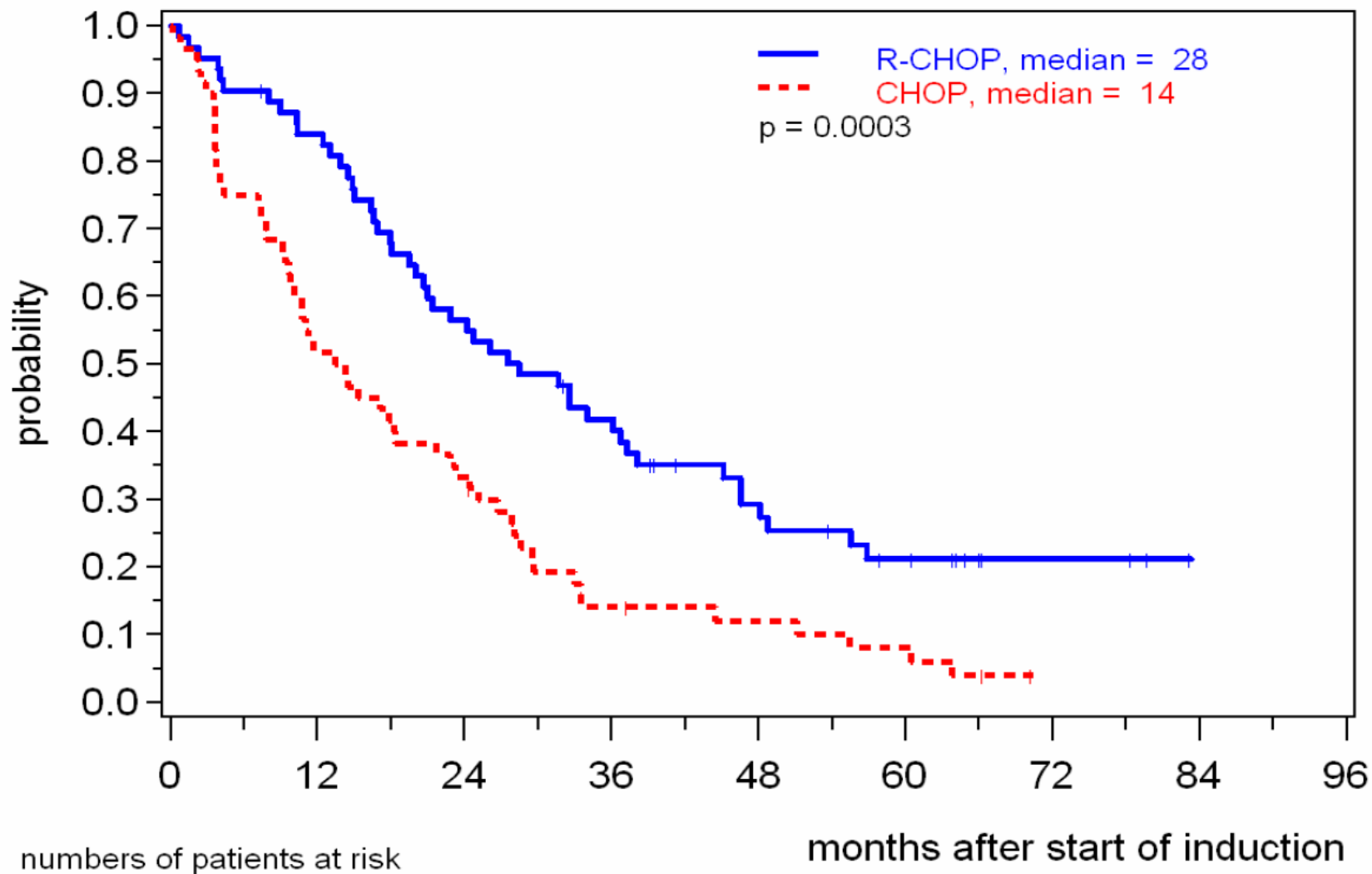
Treatment Options in the Younger Patient

- 55-year-old male
- no B-symptoms
- leukocytes 7.500 / μ l
- LDH upper limit (239 U/l)
- stage IVa MCL (abdominal nodes >4 cm, colon, bone marrow)

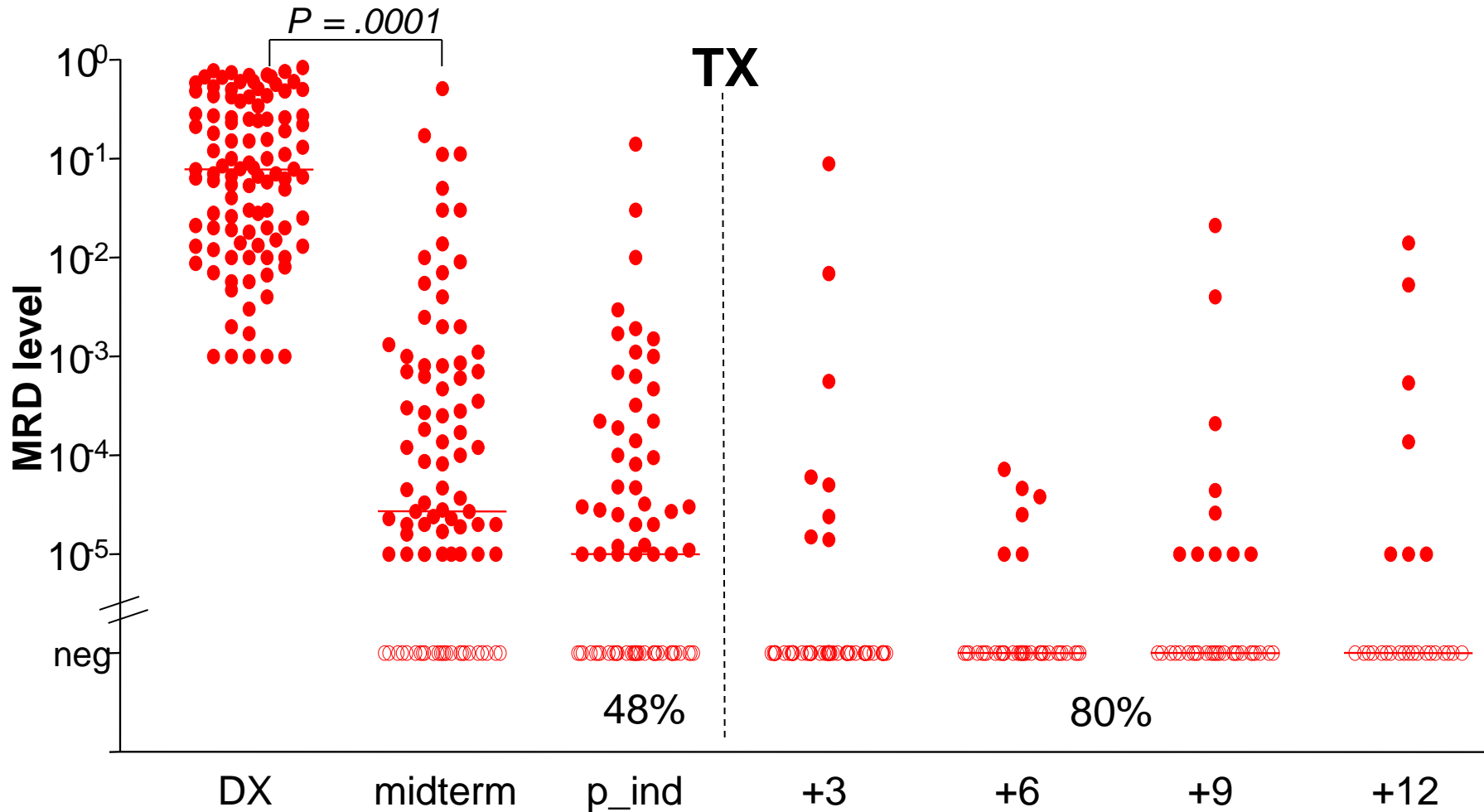
Table 7. Simplified prognostic index

Points	Age, y	ECOG	LDHULN	WBC, 10 ⁹ /L
0	<50	0-1	<0.67	< 6.700
1	50-59	—	0.67-0.99	6.700-9.999
2	60-69	2-4	1.000 - 1.49	1.000-14.999
3	\geq 70	—	\geq 1.5000	\geq 15000

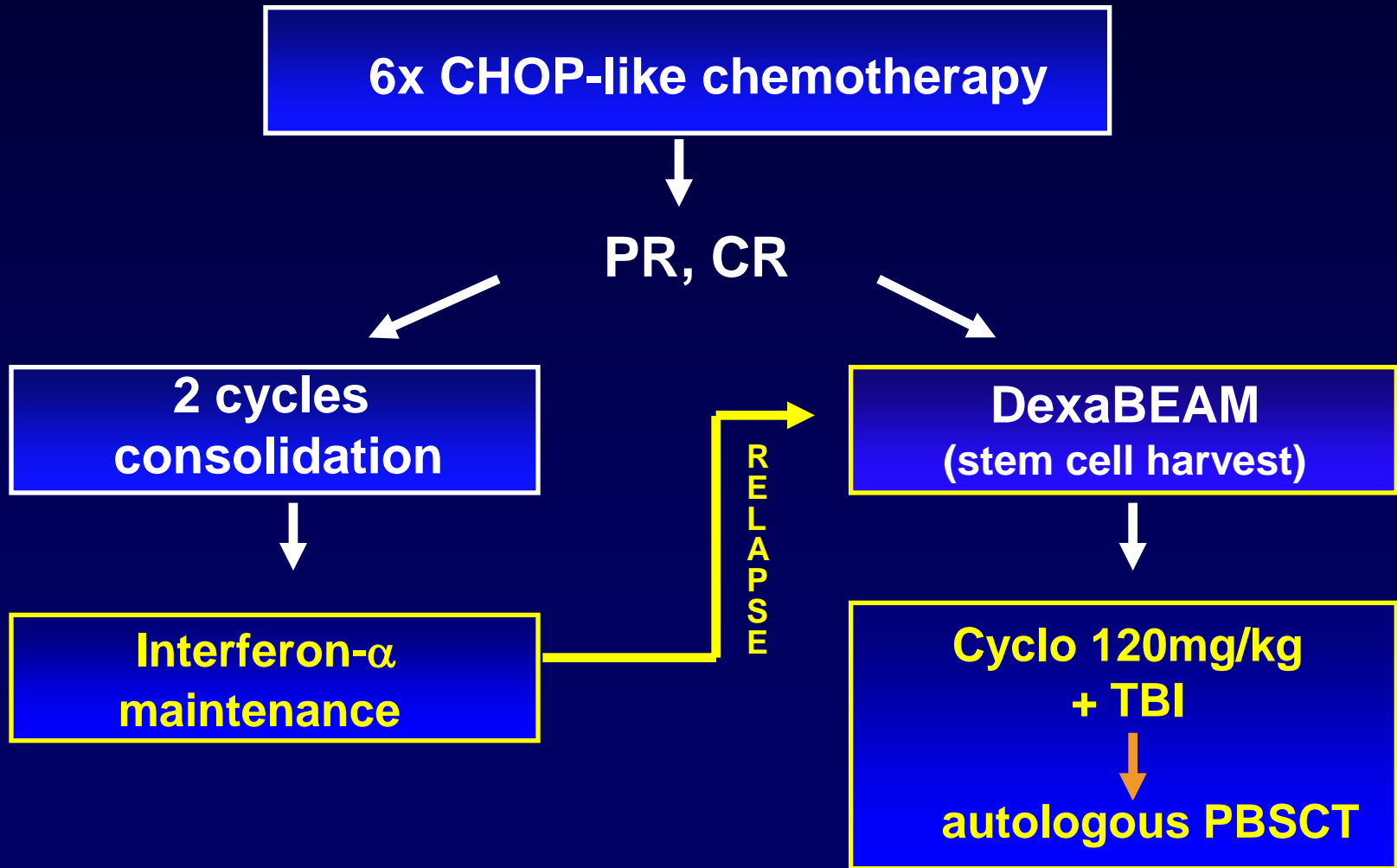
CHOP vs. R-CHOP: MCL Time to Treatment Failure



MCL Younger MRD (n = 109)

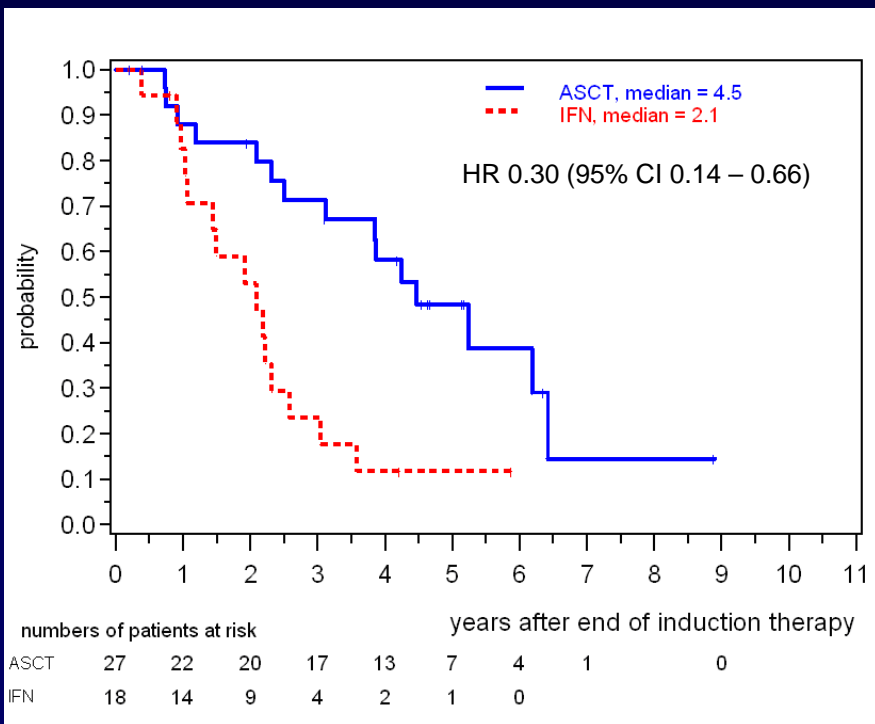


European MCL Network ASCT vs. IFN

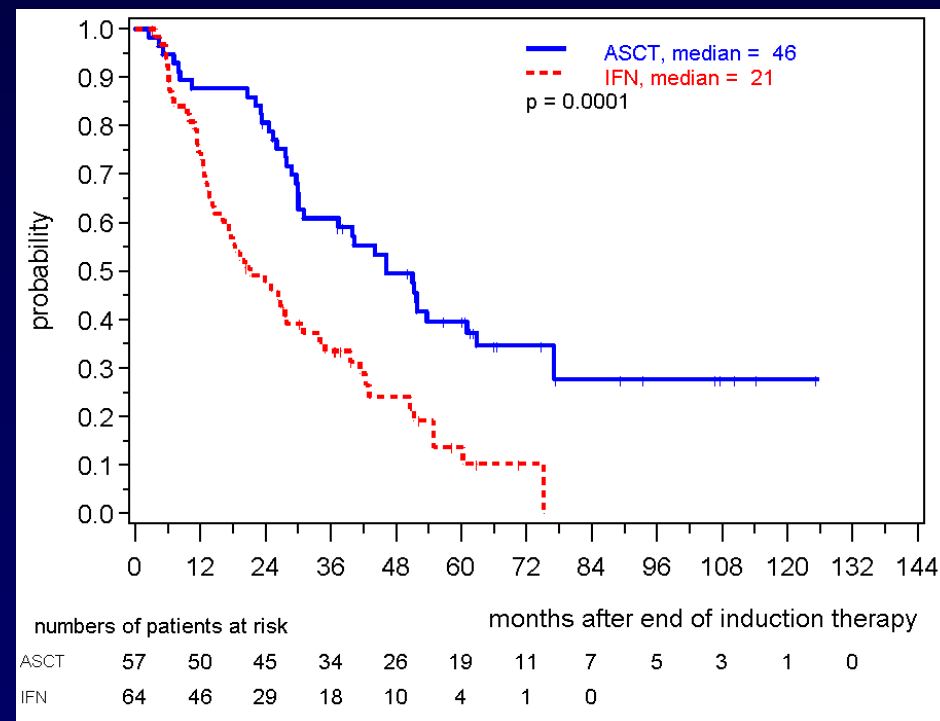


Mantle Cell Lymphoma Progression-Free Survival

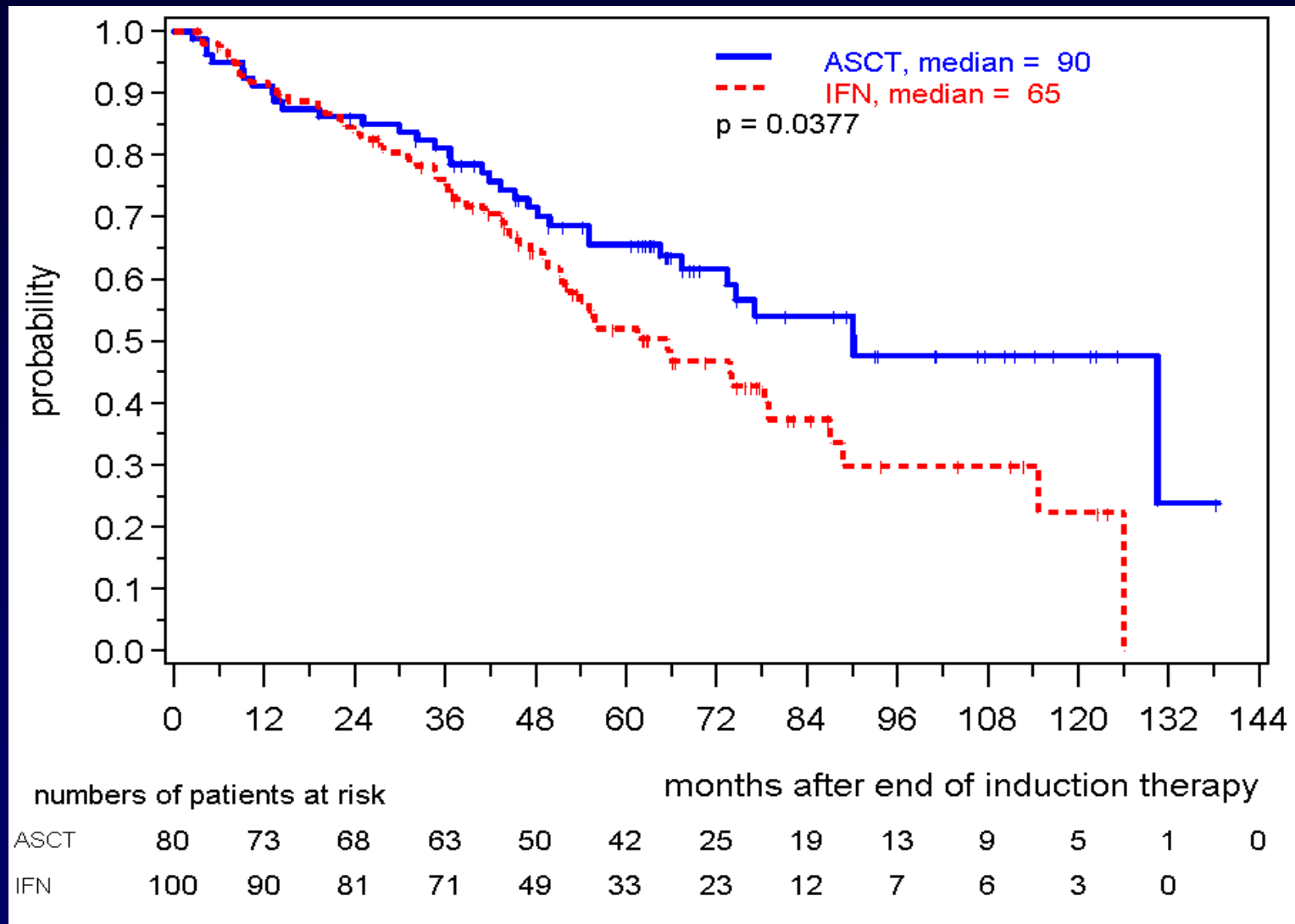
CR after induction only



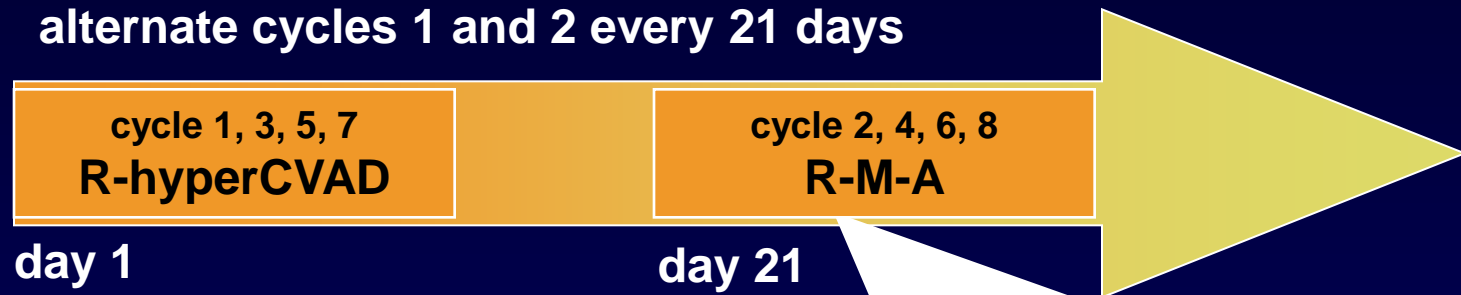
Low risk MIPI



Univariate Analysis: ASCT vs. IFN Overall Survival



Rituximab + HyperCVAD/M-A in MCL



Rituximab $375\text{mg}/\text{m}^2$ (day 1)

Methotrexate $200\text{mg}/\text{m}^2$ i.v. 2 hours (day 2)

Methotrexate $800\text{mg}/\text{m}^2$ i.v. continuous 22 h (day 2)

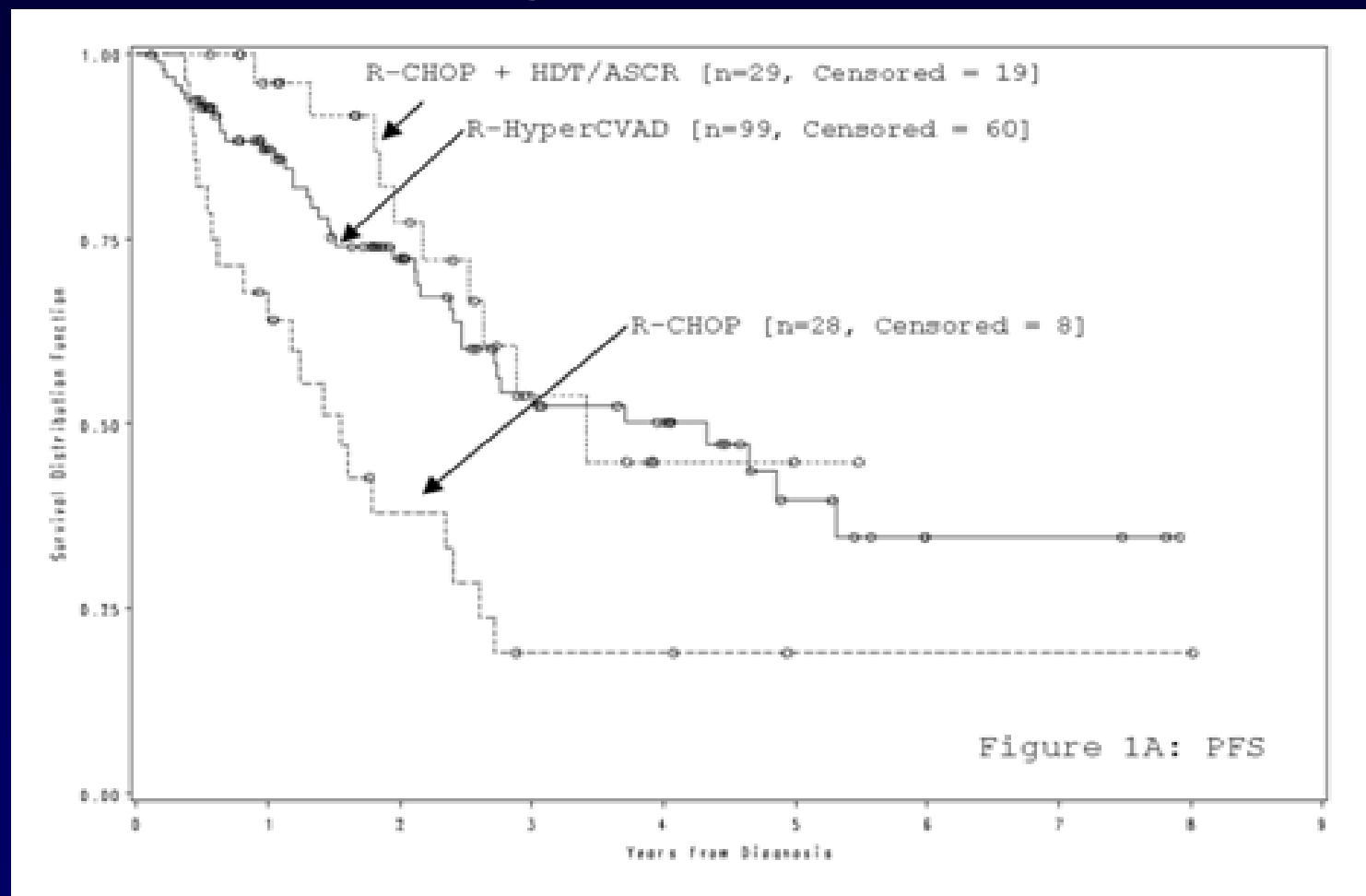
Cytarabine $1,000/3,000\text{mg}/\text{m}^2$ i.v. 2x 2h (days 3–4)

antifungal, antibacterial, antiviral prophylaxis: G-CSF !!!

Dose-Intensified Regimens in MCL

R-CHOP vs. R-CHOP+ASCT / R-HyperCVAD

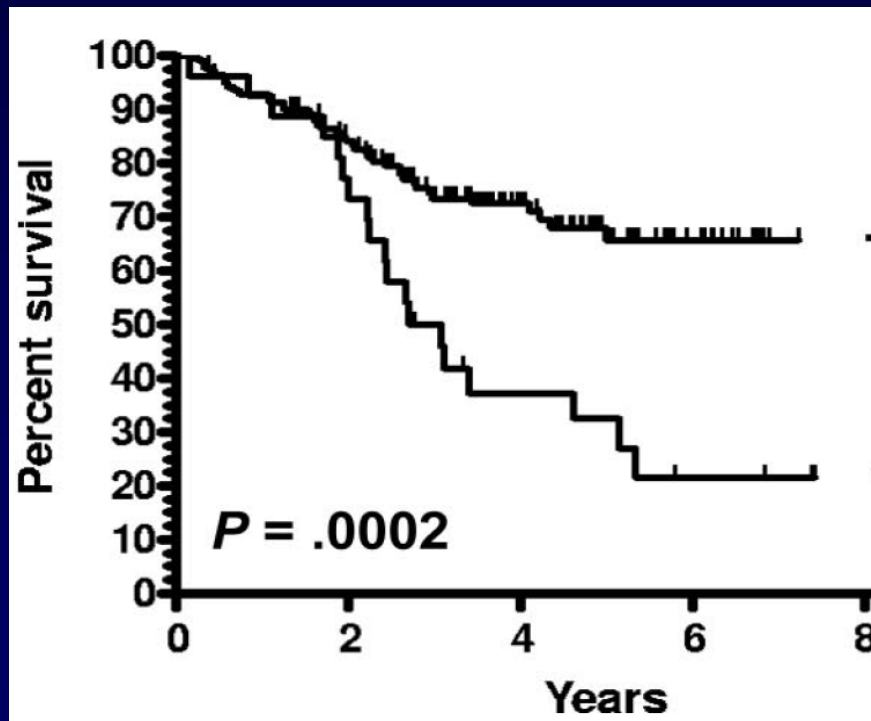
Progression-free survival



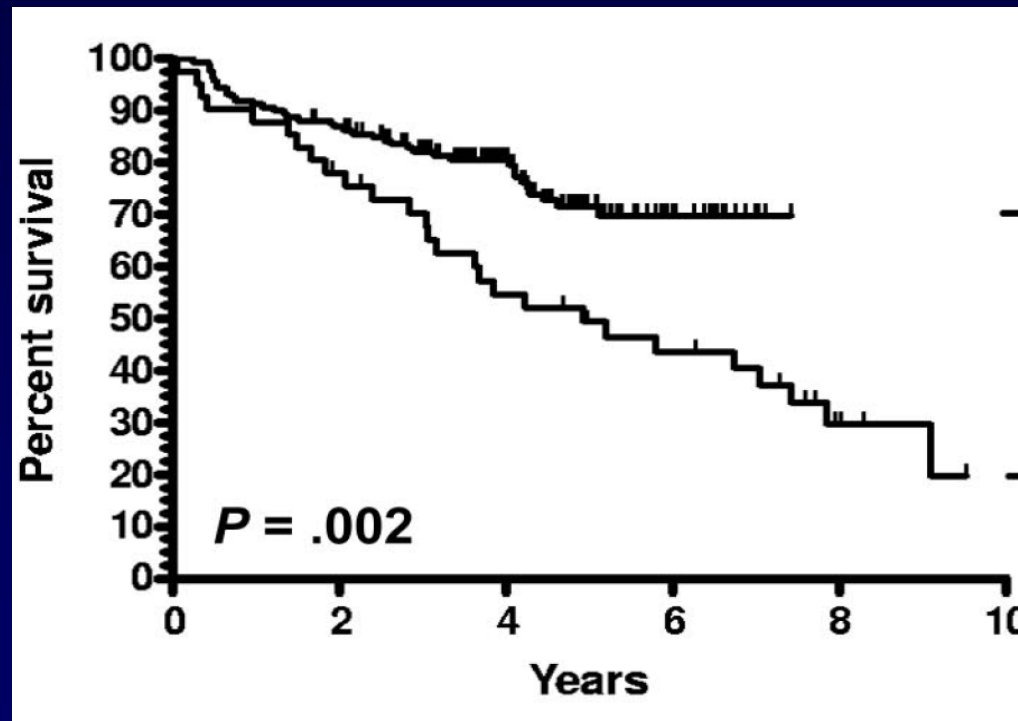
Mantle Cell Lymphoma

R-CHOP/High-Dose Ara-C => ASCT

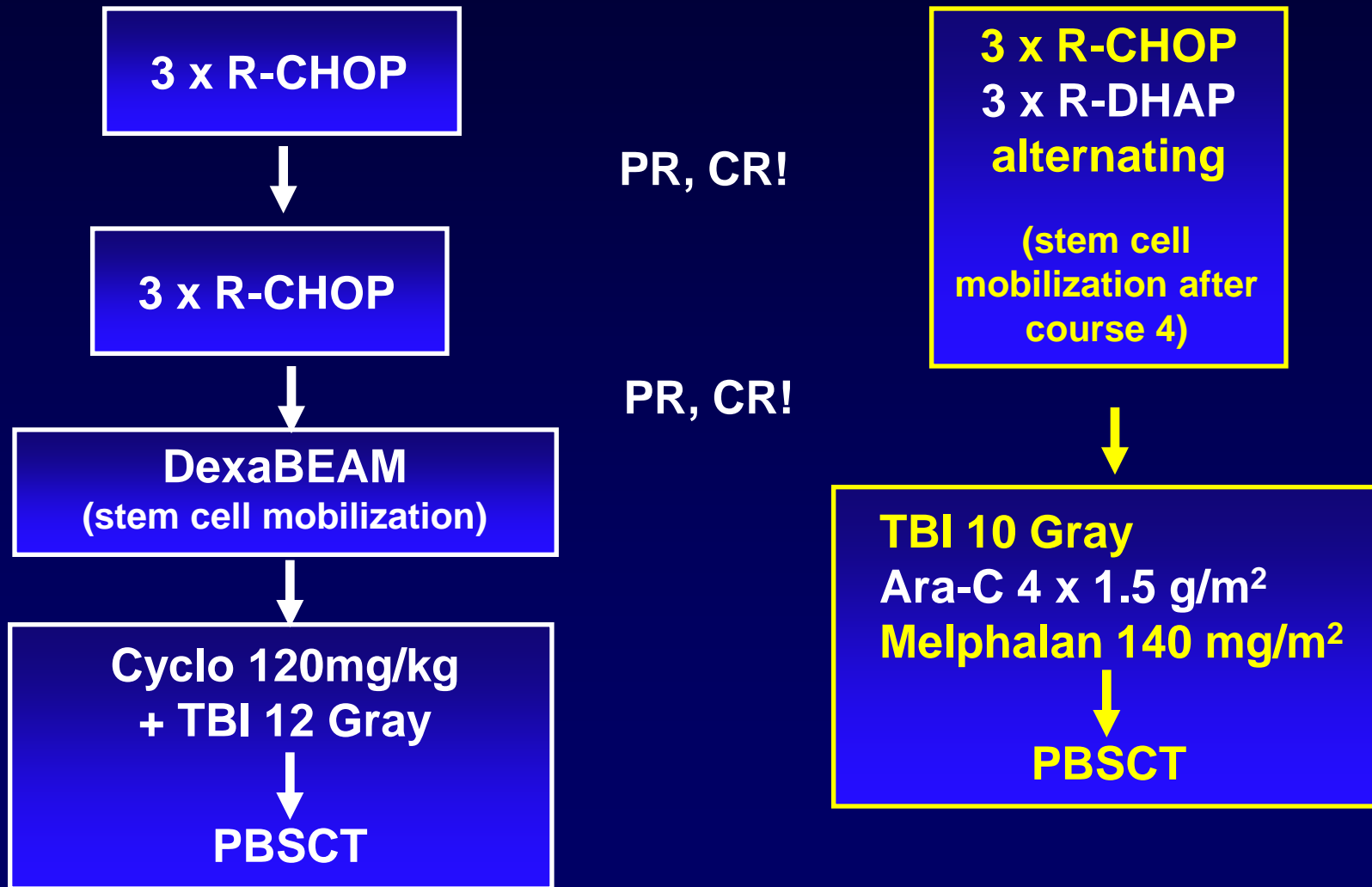
Progression-free survival



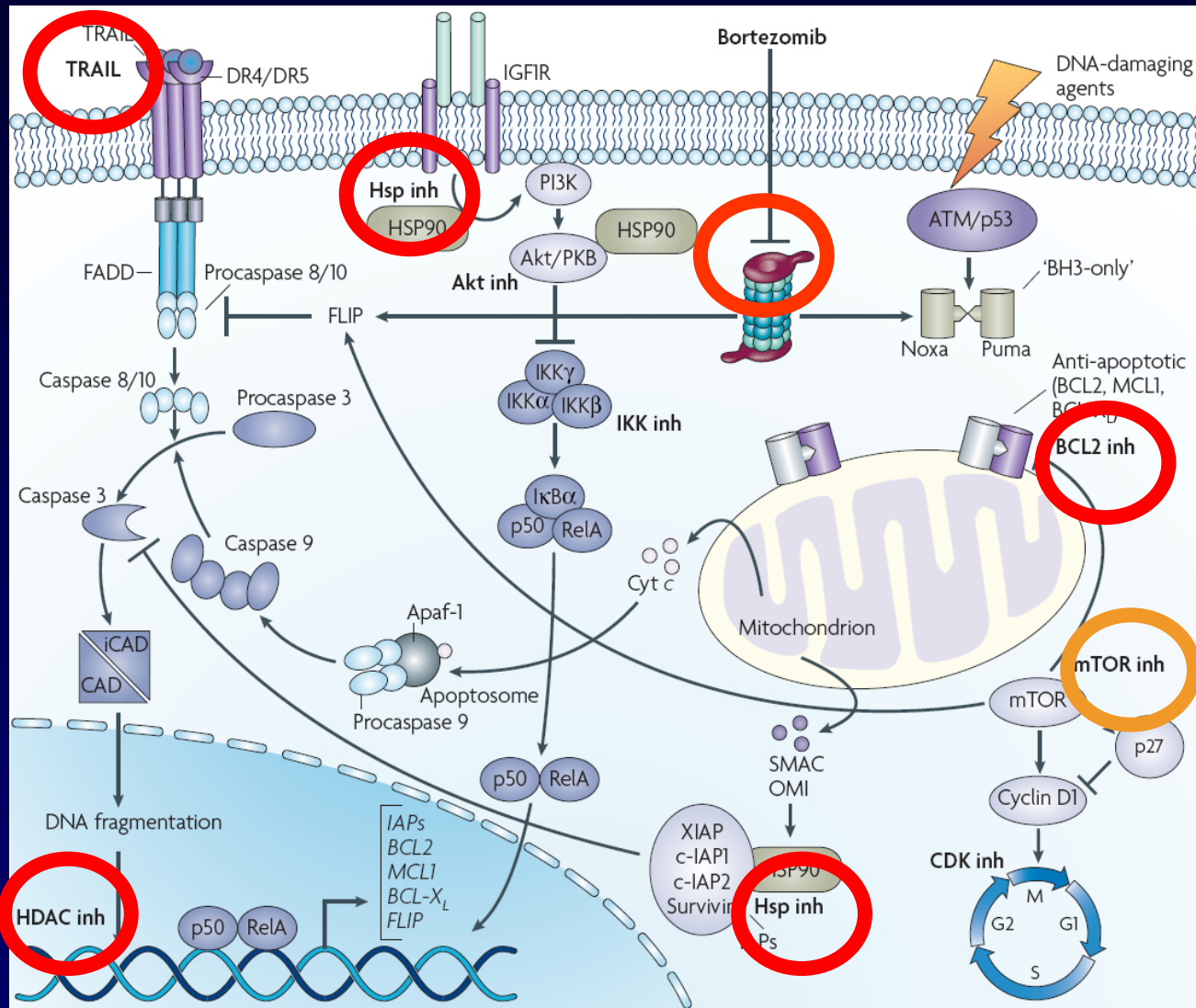
Overall survival



European MCL Network Patients <65 Years



Altered Pathways in MCL



Radioimmunotherapy in MCL

Comparison of Molecules

Table 2. Activity of Selected Single Agents in Relapsed or Refractory MCL

Single Agent	No. of Patients With Prior Rituximab Therapy	%	Response Rate (%)	CR (%)	Median EFS/ PFS (months)	Study
Rituximab	12	0	33	NR	NR	Coiffier et al ¹⁹
Rituximab	35	0	37	14	NR	Foran et al ²⁰
⁹⁰ Y-Ibritumomab tiuxetan	35	91	32	16	6	Wang et al*
Temsirolimus	34	89	38	3	6.5	Witzig et al ²¹
Bortezomib	144	96	33	8	6.2	Fisher et al ¹⁶
R-Bendamustin e	12	56	92	41	19 (DR)	Robinson 09
R-Bendamustin e	16	0	75	25	18	Rummel 09

young patient (<65)

elderly patient (>65)

compromised patient

First line treatment

dose-intensified
immuno-chemotherapy
(either sequential:
e.g. R-CHOP =>PBSCT
or R-Hyper-CVAD)

conventional
immuno-chemotherapy
(e.g. R-CHOP)
↓
Rituximab maintenance ?
radioimmunotherapy ?

watch & wait ?
Rituximab monotherapy
Chlorambucil
Bendamustine

1. relapse

high tumor load:
immuno-chemotherapy
(e.g. R-FC)
↓
allo-transplant ?
radioimmunotherapy ?
rituximab maintenance ?

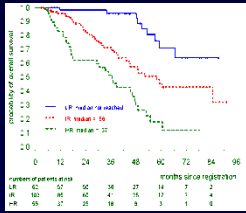
immuno-chemotherapy
(e.g. R-FC,
R-Bendamustine)
↓
molecular approaches ?
autologous PBSCT
radioimmunotherapy ?
rituximab maintenance ?

immuno-
chemotherapy
(e.g.
R-Bendamustine)
molecular approaches

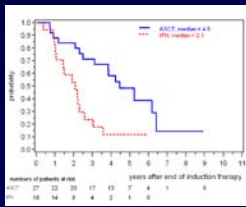
higher relapse

molecular approaches: Bortezomib, Tamsirolimus, Thalidomide/
Lenalidomide, Flavopiridol (**preferable in combination**)
repeat previous therapy (long remissions)

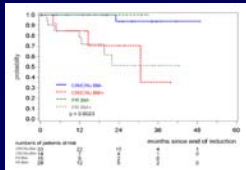
Mantle Cell Lymphoma Clinical Management



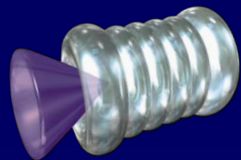
- clinical course is variable (MIPIb)



- younger patients: dose intensification (relapse: allogeneic transplantation)



- MRD may guide future therapies



- In studies: multimodal molecular strategies



Annual Conference in Jerusalem

