

LYMPHOMAS WITH GOOD PROGNOSIS: DO NOT HARM

FOLLICULAR LYMPHOMA

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ROMA
HEMATOLOGY
CONFERENCE
the lymphomas

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Hotel nhow Roma

Disclosure Silvia Montoto: none

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

Outline

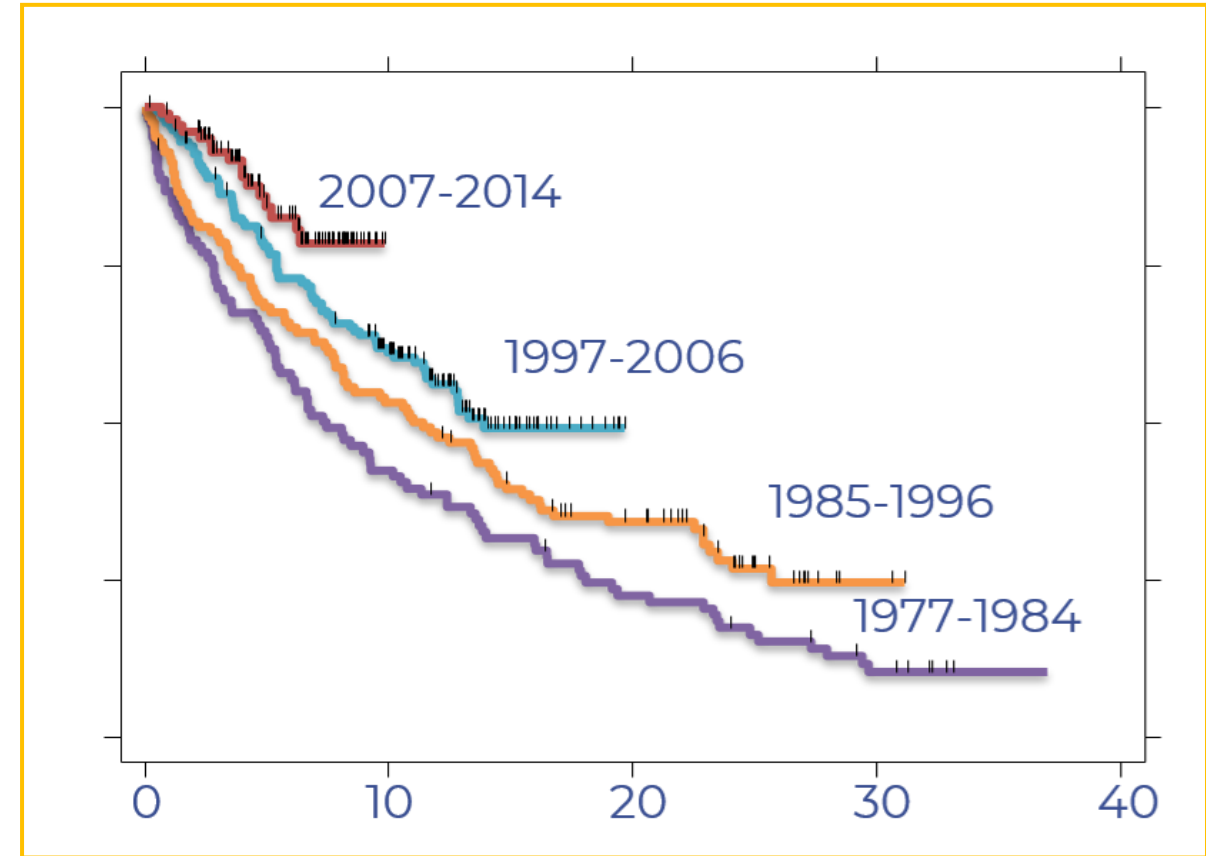
- Natural history and clinical course of FL
- Objectives of treatment
- Results

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Natural history and clinical course of FL

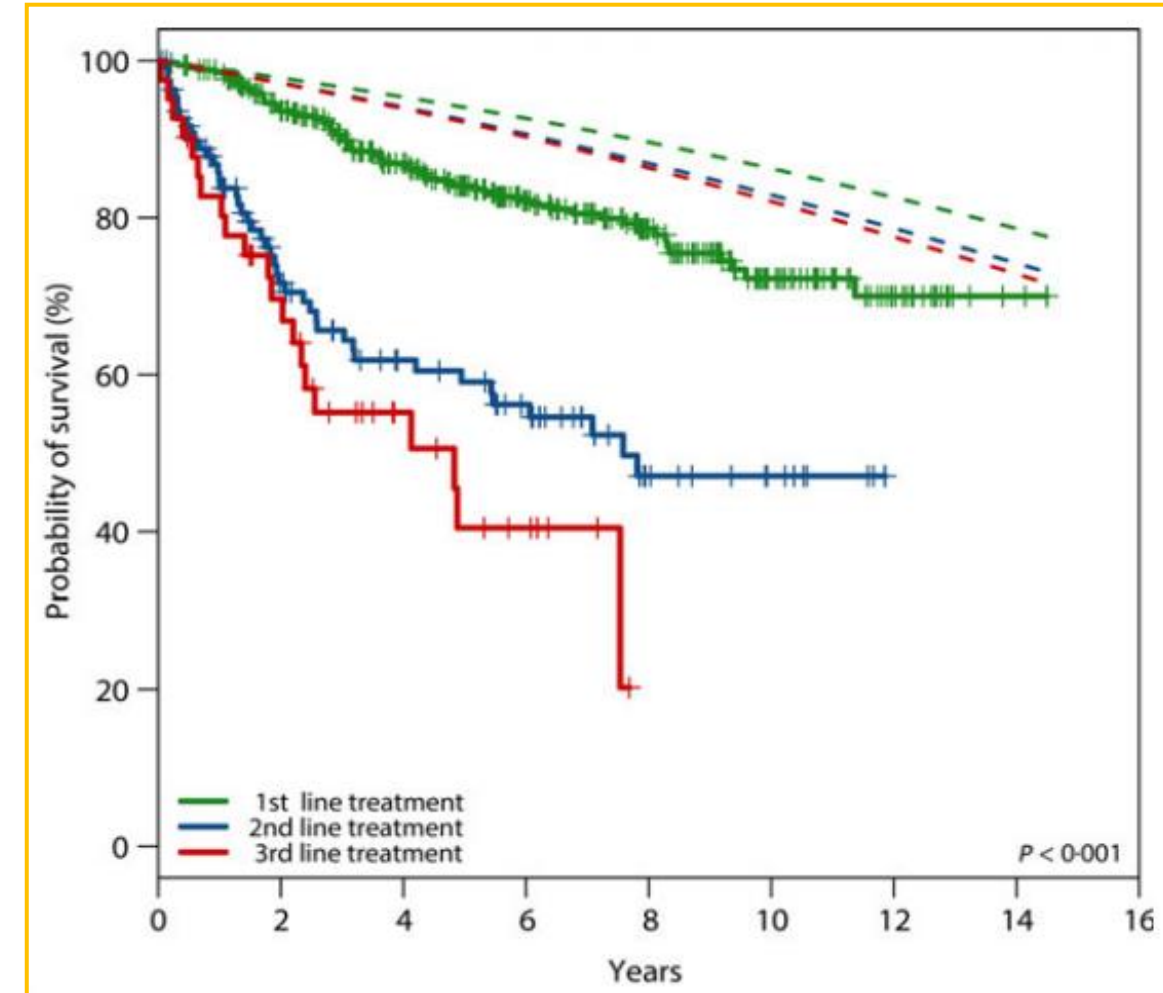
- Long survival
- Multiple relapses
- Risk of histological transformation
- Incurable (with conventional treatment)



St Bartholomew's hospital 1977-2014

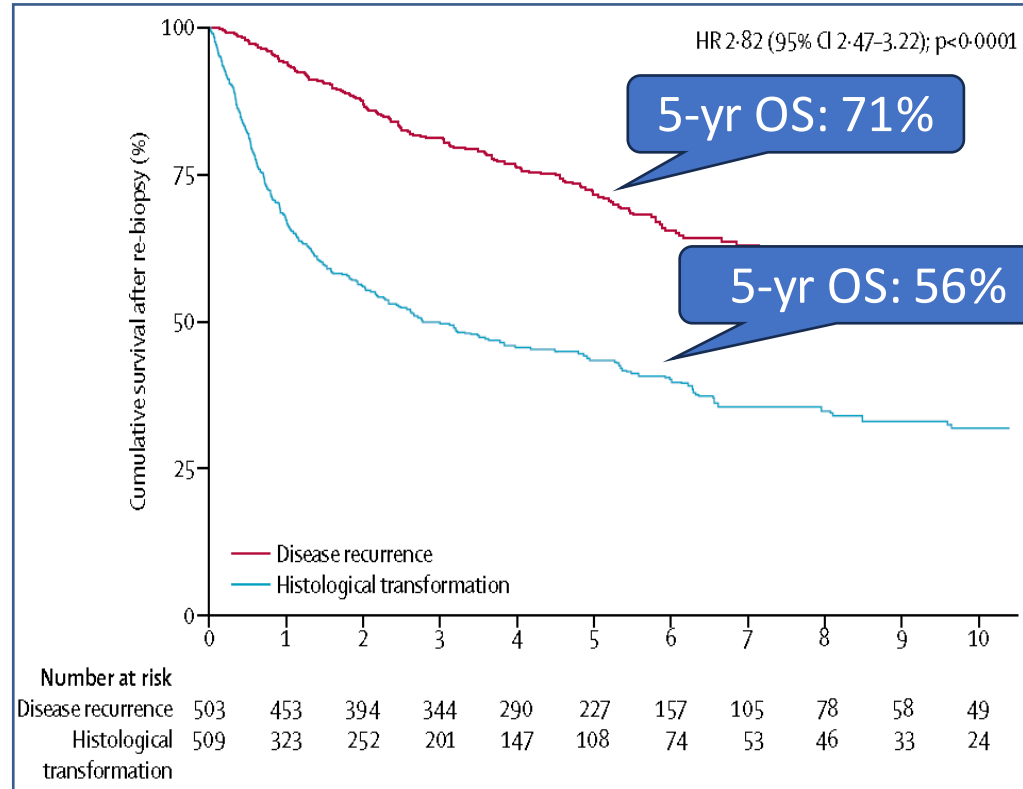
Outcome at each relapse

	Median DOR	5-yr DOR	Median PFS
After L1	NR	62%	10.4 yrs
After L2	3.1 yrs	39%	2.4 yrs
After L3	2.1 yrs	24%	2 yrs

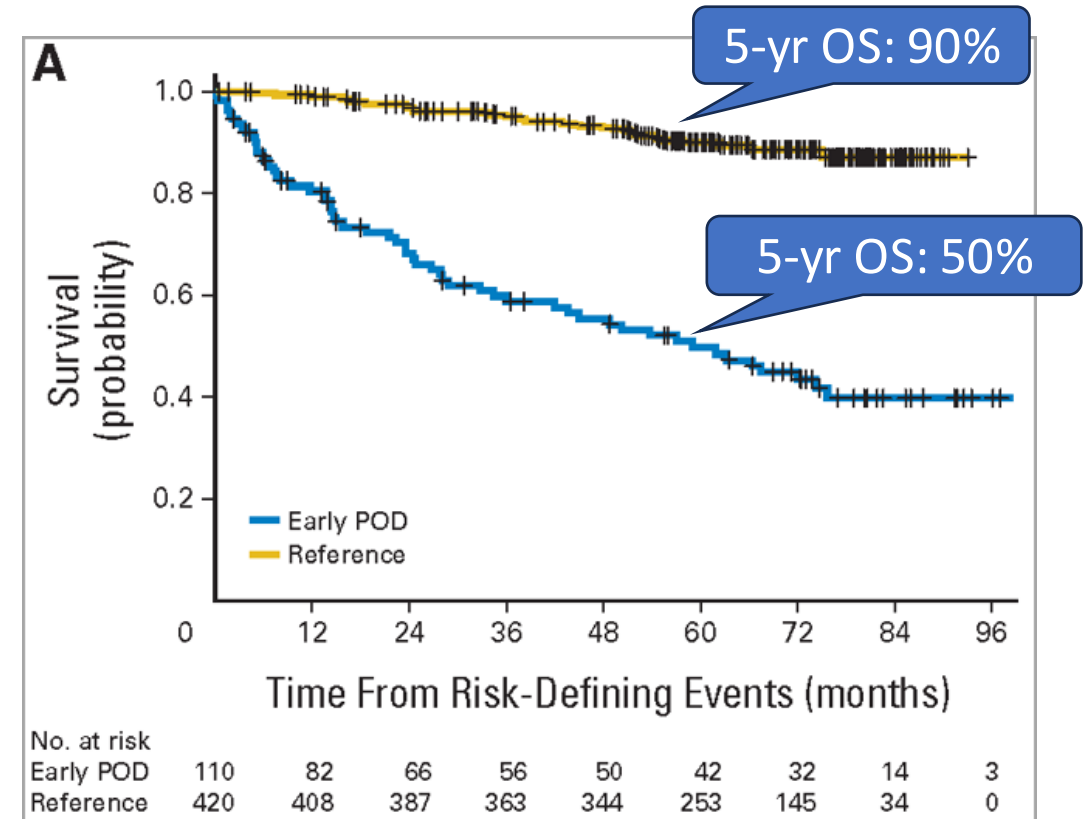


Rivas-Delgado A et al, Br J Haematol, 2018

High-risk patients: transformed FL or POD24

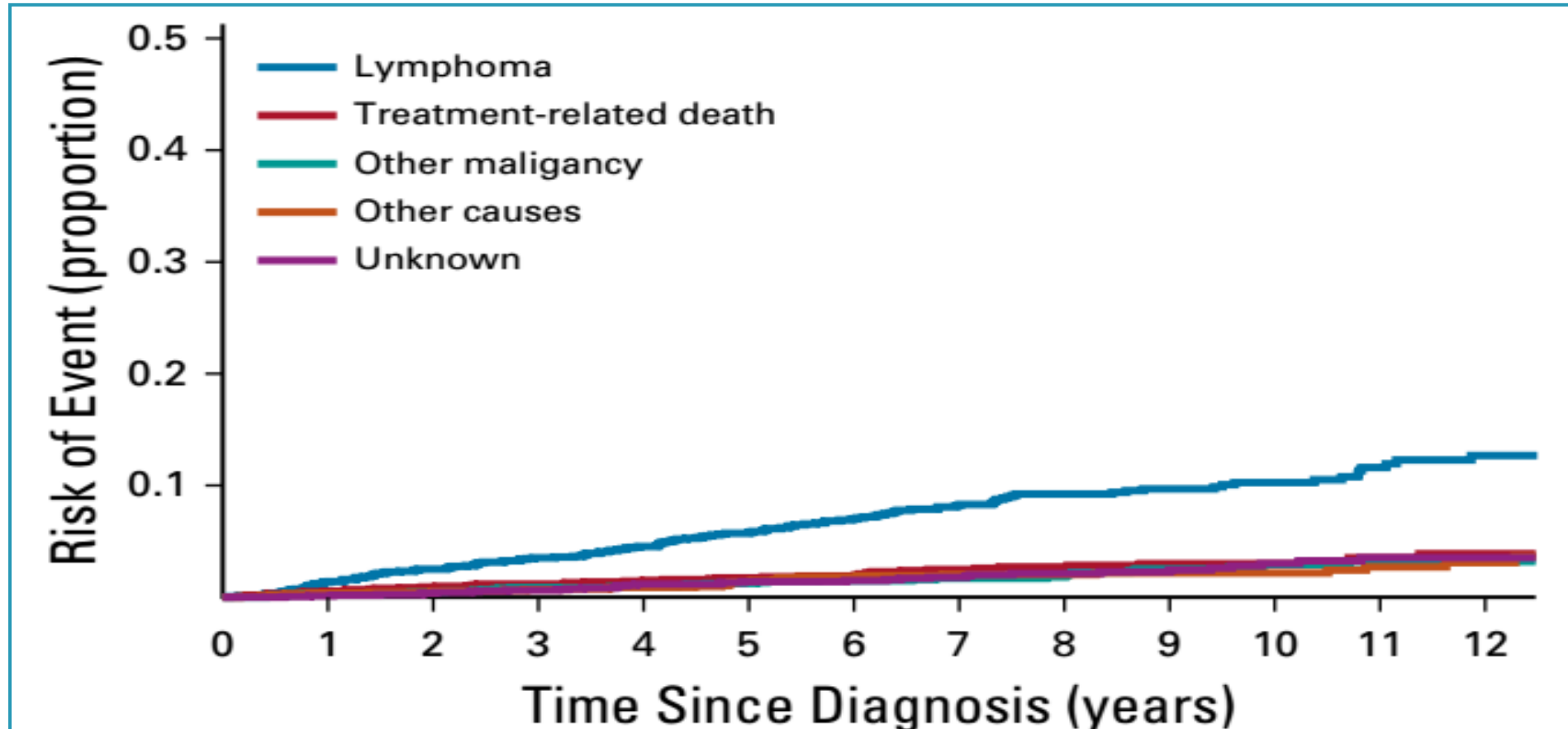


Federico M et al, Lancet Haematol, 2018



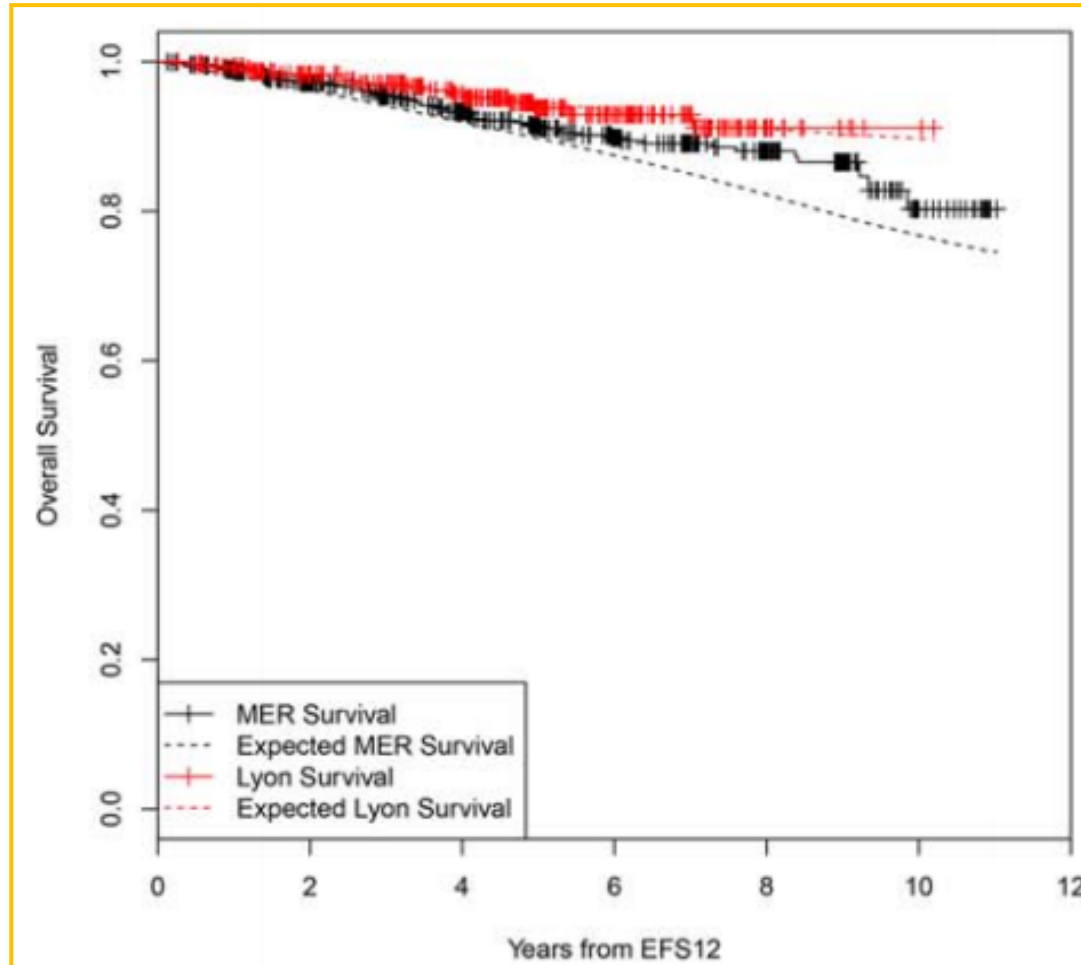
Casulo C et al, J Clin Oncol, 2015

Causes of death in patients with FL



Sarkozy C et al, J Clin Oncol, 2018

Good-risk patients: EFS12



Maurer M et al, Am J Hematol, 2016

Information we give at diagnosis

- Diagnosis: cancer
 - Advanced stage
 - Maybe fatal (but not immediately)
 - There are treatments, but it's difficult to cure
-
- however, you don't need any treatment at the moment

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Objectives of treatment: what patients want

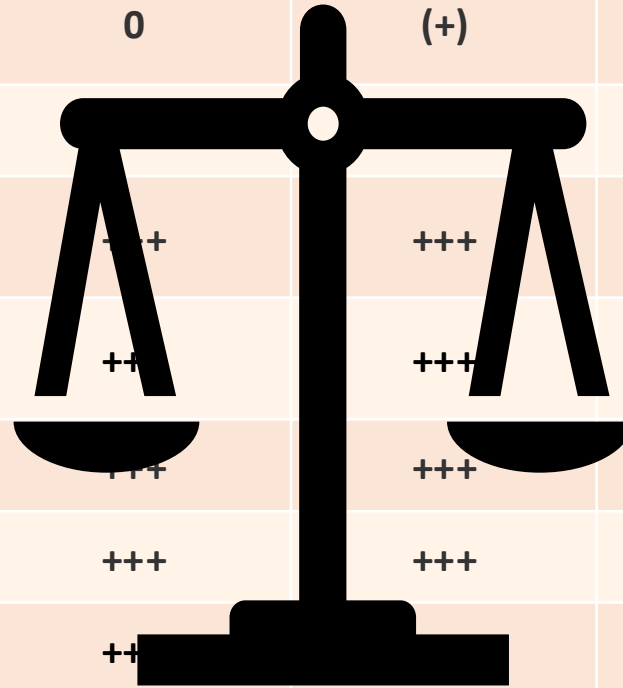
- A life without disease
- A life not shortened by the disease (or its treatment)
- A better life, without signs or symptoms
- A better life, without complications of the disease or the treatment
- A normal life, at home as much as possible

Objectives of treatment and what doctors measure

- To cure - DFS
- To prolong survival - OS
- To prolong response duration - PFS, RD
- Symptomatic improvement - QoL
- To reduce the risk of HT (in patients with FL) - 'TFS'

Effects and results of treatment in patients with FL

	Morbidity	Mortality	Symptomatic improvement	Response rate	Prolonged response	Cure	Response in high-risk patients
Expectant management	0	0	0	(+)	0/+	0	0
Anti-CD20	+	0			+	0	0
Immuno-chemotherapy	++	+	+++	+++	+++	?	-
Chemo-free regimens	++	+	+++	+++	+++	?	+
ASCT	+++	++	+++	+++	+++	++	+
Allo-SCT	++++	+++	+++	+++	+++	++	+
CAR-T/bispecifics	++	+/++	++		+++	?	++



Adapted from E Montserrat, Hospital Clínic, Barcelona

Outline

- Natural history and clinical course of FL
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Benefits of immediate treatment vs expectant management

- Prolongs 'response duration'
- Does not prolong survival
- Does not impact on the risk of HT
- Improves QoL?

A life without signs, symptoms or toxicity: does W&W impair QoL?

- There is an improvement in QoL over time in some domains, both in W&W and R+R
- In some of the domains the improvement is bigger in the R+R arm
- There is no worsening in any of the domains in the W&W arm (nor in the R+R arm)
- Worries about the lymphoma becoming more aggressive: improved/stayed low in 59% in W&W vs 81% in R+R
- Worries about the lymphoma needing (more) treatment: improved/stayed low in 59% in W&W vs 76% in R+R

Marzolini M et al, Br J Haematol, 2025

A better life: does chemo-free equals toxicity-free?

Phase 2 study of idelalisib and entospletinib: pneumonitis limits combination therapy in relapsed refractory CLL and NHL

Paul M. Barr,¹ Gene B. Saylor,² Stephen E. Spurgeon,³ Bruce D. Cheson,⁴ Daniel R. Greenwald,⁵ Susan M. O'Brien,⁶ Andre K. D. Liem,⁷ Rosemary E. McIntyre,⁸ Adarsh Joshi,⁹ Esteban Abella-Dominicis,⁹ Michael J. Hawkins,⁹ Anita Reddy,⁹

Lenalidomide, idelalisib, and rituximab are unacceptably toxic in patients with relapsed/refractory indolent lymphoma

Chan Yoon Cheah, Loretta J. Nastoupil, Sattva S. Neelapu, Sheryl G. Forbes, Yasuhiro Oki and Nathan H. Fowler

Phase I trial of rituximab, lenalidomide, and ibrutinib in previously untreated follicular lymphoma: Alliance A051103

Chaitra S. Ujjani, Sin-Ho Jung, Brandelyn Pitcher, Peter Martin, Steven I. Park, Kristie A. Blum, Sonali M. Smith, Myron Czuczman, Matthew S. Davids, Ellis Levine, Lionel D. Lewis, Scott E. Smith, Nancy L. Bartlett, John P. Leonard and Bruce D. Cheson

Blood 2016 :blood-2016-06-718106; doi:10.1182/blood-2016-06-718106

factors prior to enrollment. Given the increased toxicity and required dose modifications, as well as the apparent lack of additional clinical benefit to the rituximab–lenalidomide doublet, further investigation of the regimen in this setting seems unwarranted. The study was registered with www.ClinicalTrials.gov (NCT01829568).



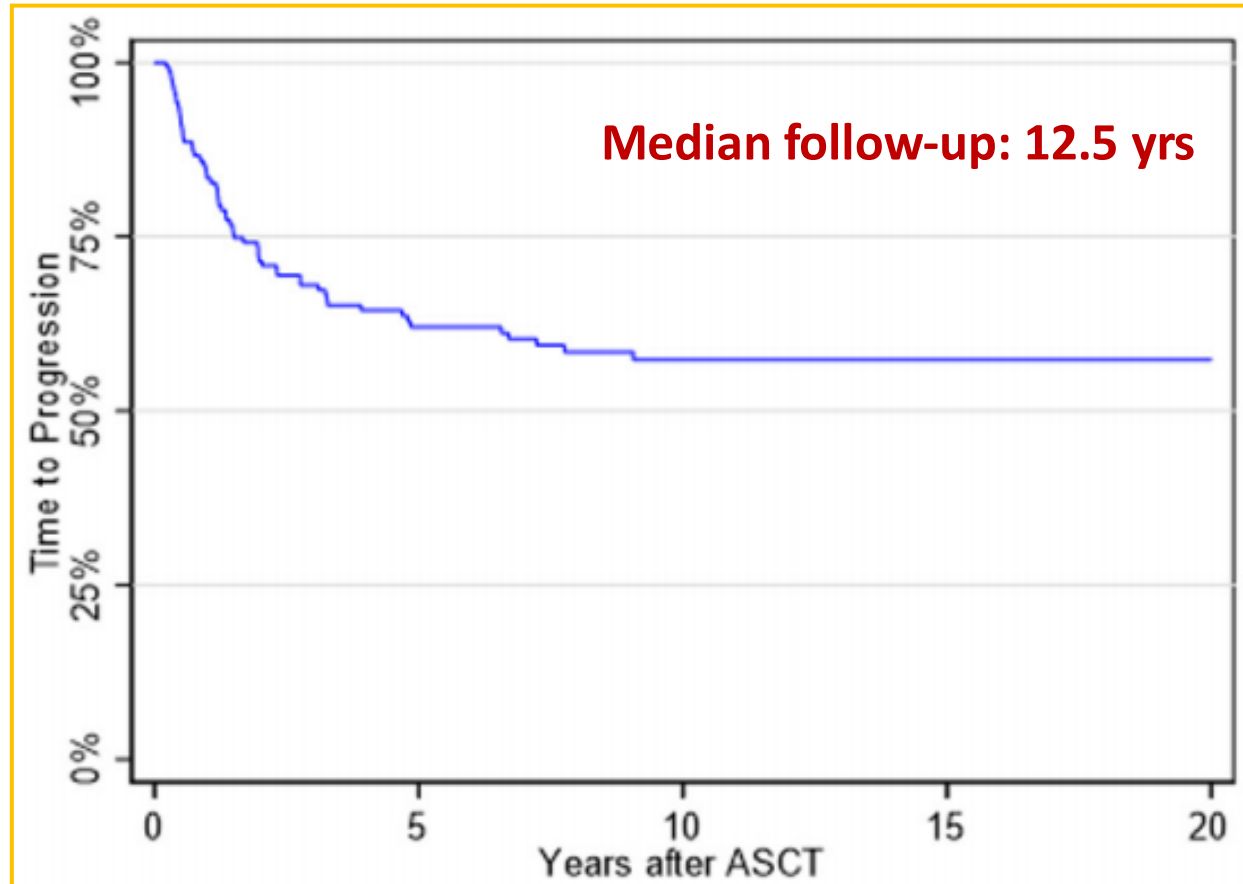
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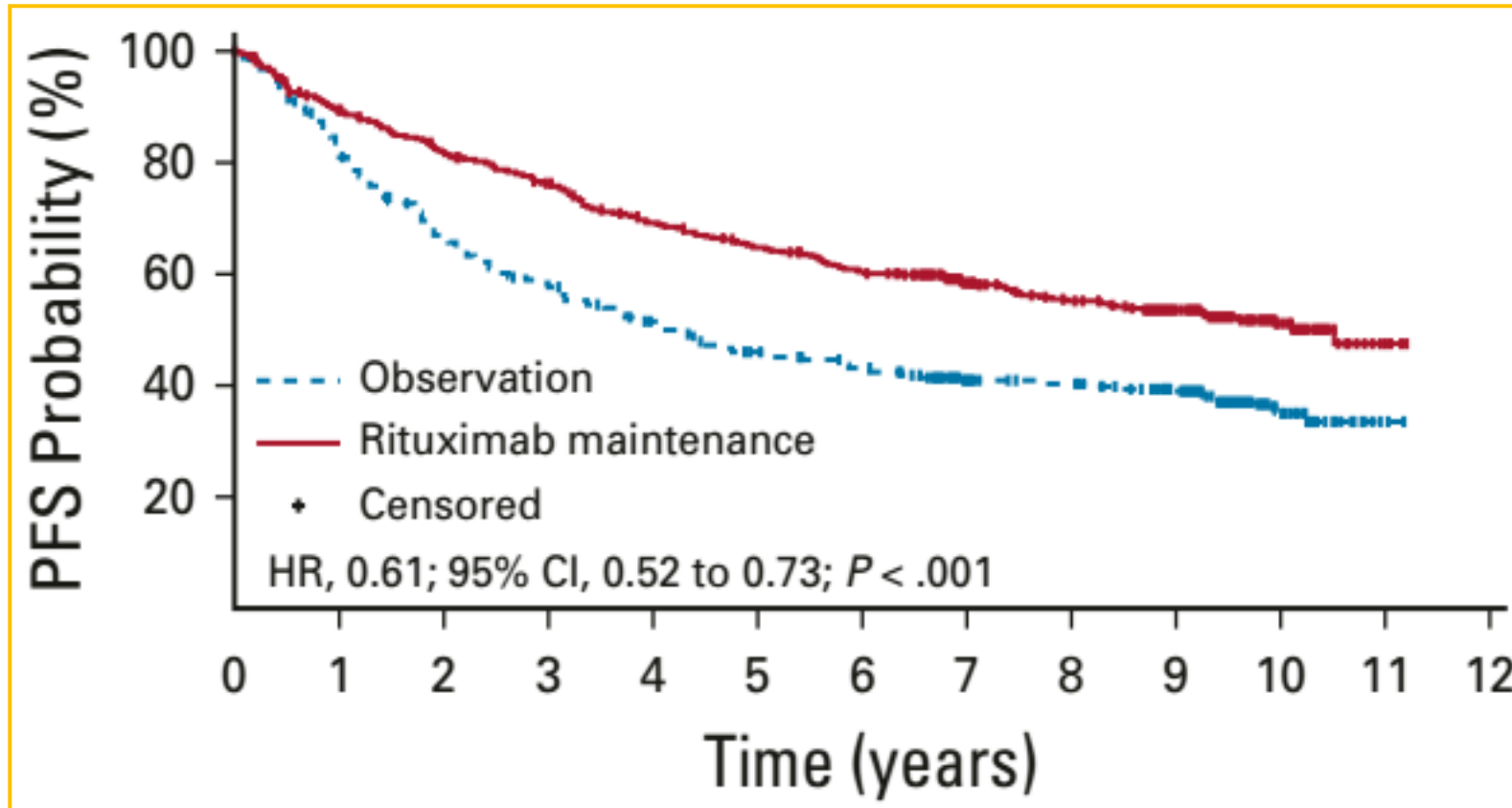
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Cure = a life free of disease (*ideally, not shortened by its treatment*)



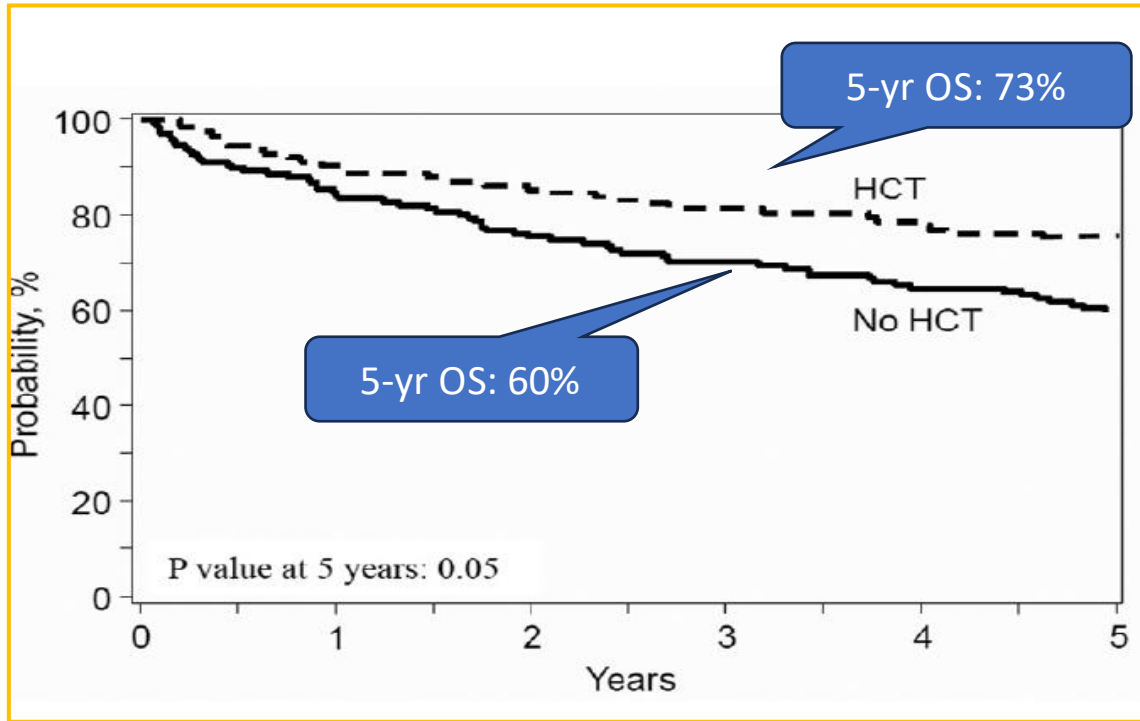
Puckrin R et al, Br J Haematol, 2023

Can immuno-chemotherapy cure FL?

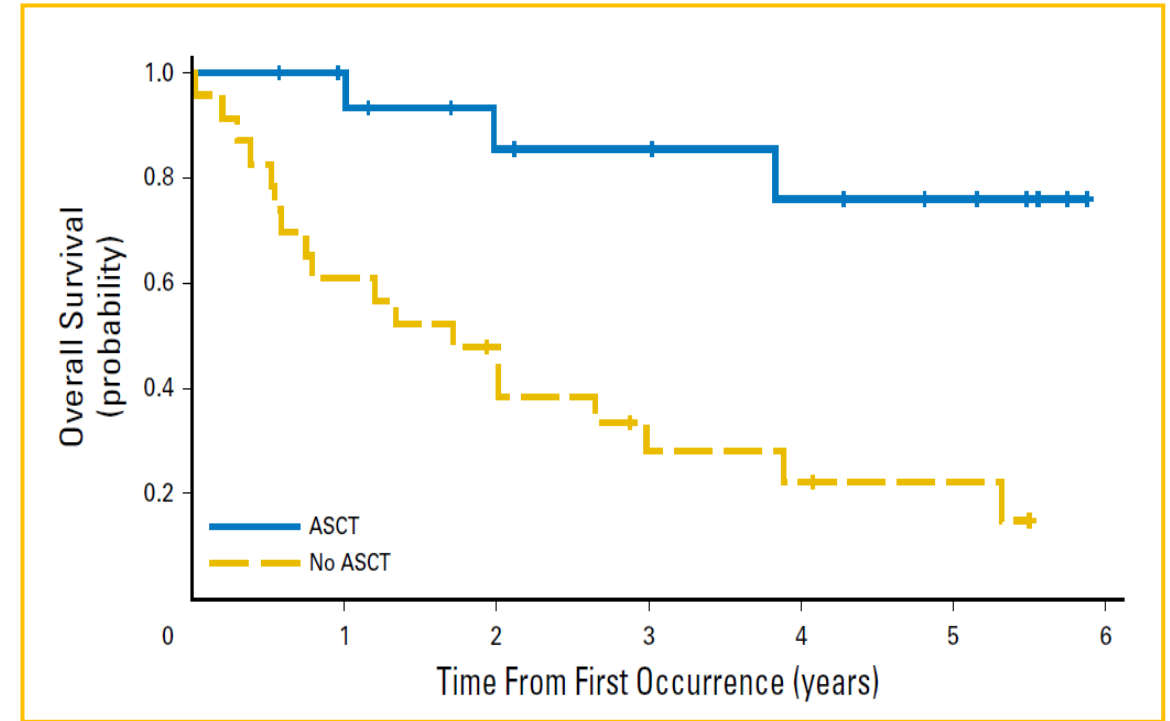


Bachy E et al, J Clin Oncol, 2019

Objective: to improve the outcome of high-risk FL (POD24 or HT)



Casulo C et al, BBMT, 2018



Sarkozy C et al, J Clin Oncol, 2016

Clinical trials of CAR-T therapy

Series, year	Phase	Indication	N (FL, infused)	Median follow-up	ORR/CR	PFS	Efficacy after ASCT	CRS (any/grade 3-5)	ICANS (any/grade 3-5)
Morschhauser, 2024 (TRASCEND)	II	R/R iNHL ≥ 2 lines	130	19 mo	97/94%	83% (at 12 mo)	12-mo PFS: 90%	58%/1%	15%/2%
Dreyling, 2024 (ELARA)	II	R/R FL ≥ 2 lines	97	29 mo	86/68%	57% (at 24 mo)	CRR: 66%	49%/0	4%/1%
Neelapu, 2025 (ZUMA-5)	II	R/R iNHL ≥ 2 lines	127 FL, 31 MZL	65 mo	90/75%	50% (at 60 mo)	36-mo PFS: 76%	78%/6%	56%/15%

Clinical trials of bi-specifics

Drug (series, year)	Phase	Indication	Schedule	N (FL)	Median follow-up	ORR/CR	PFS	CRS (any/grade 3-5)	ICANS (any/grade 3-5)
Mosunetuzumab (Budde, 2022)	II	R/R FL ≥ 2 lines	21-day cycles, max 17 (IV)	90	18 months	80/60%	47% (at 18 months)	44%/2%	3%/0
Epcoritamab (Limton, 2024)	II	R/R iNHL ≥ 2 lines	28-day cycles until progr (SC)	128	17 months	82/62%	49% (at 18 months)	49%/0	0
Odronextamab (Kim, 2024)	II	R/R NHL ≥ 2 lines	21-day cycles until progr (IV)	128	20 months	80/73%	46% (at 24 months)	57%/2%	<1%/0

A better life: toxicity, tolerability, QoL

- ASCT: unpleasant toxicity, ~4 weeks hospital admission
- Allo-SCT: GVHD
- CAR-T: CRS, ICANS
- Bi-specifics: long treatment/treatment until progression

CONCLUSIONS

- Multiple treatment options available, appropriate at different stages of the disease, appropriate for different patients
- Establish *real* aims of treatment
- Lay out realistic expectations
- Honest discussion of statistical results
- Manage the fear and anxiety associated with the diagnosis of cancer (*but not with chemotherapy!*)

Thank you!!



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