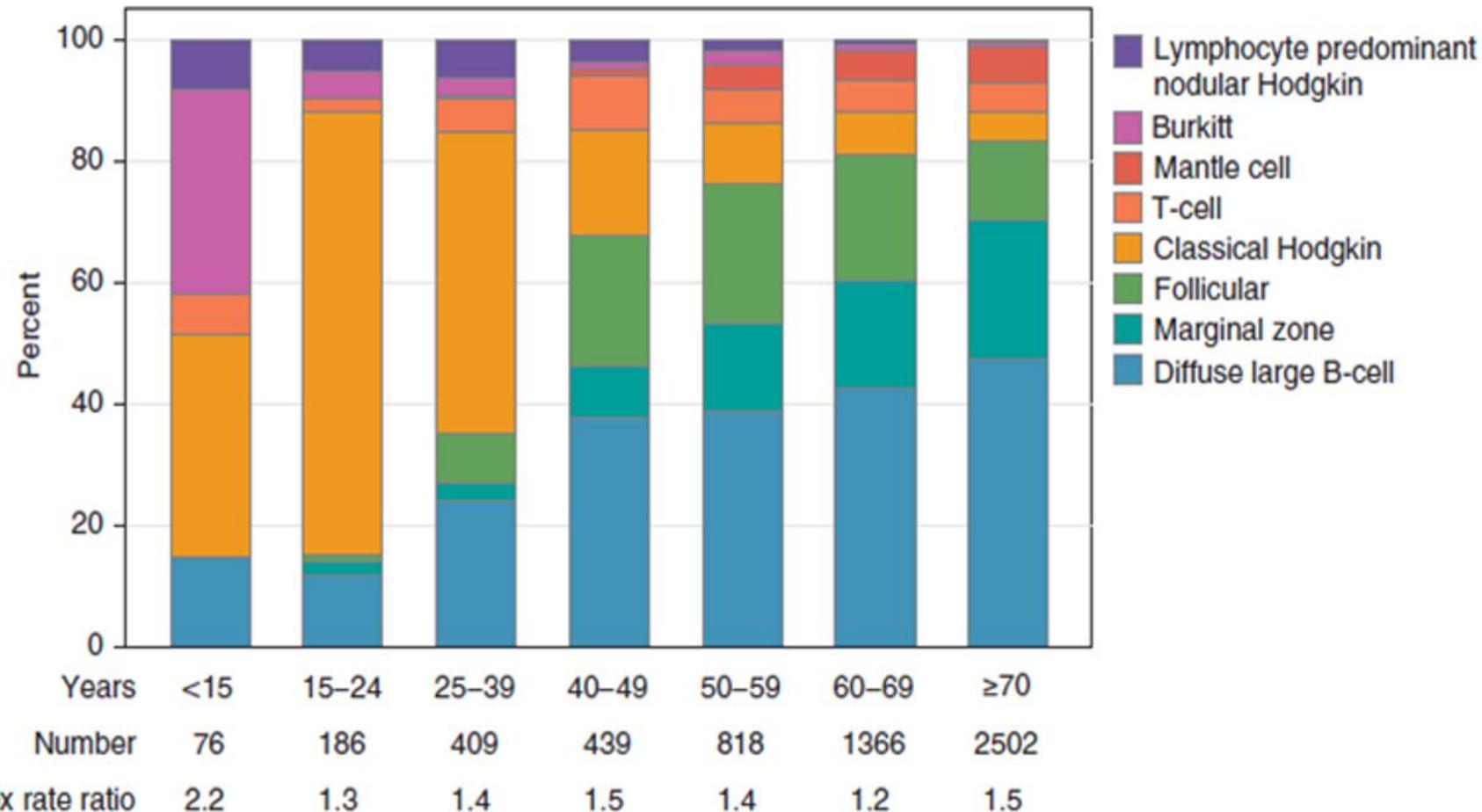


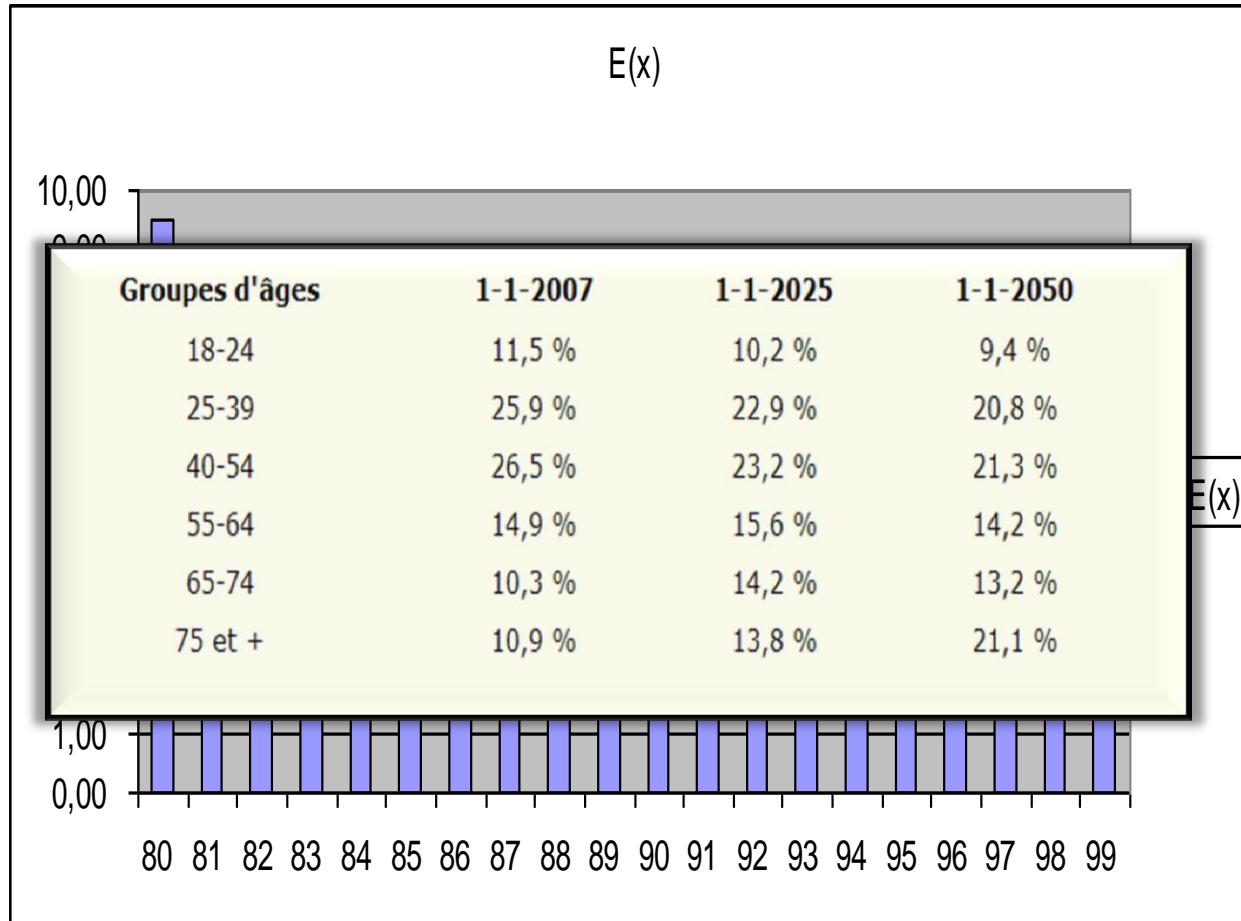
# Le Lymphome du sujet âgé est un lymphome comme les autres.

Monaco Age Oncologie

*9 mars 2017*

# Répartition des sous-types histologiques en fonction de l'âge





# Lymphome agressif au diagnostic

	98-5 (n=202 RCHOP arm)	03-7B (n=150 R-miniCHOP)	09-7B (n=120 pp OFA-mini CHOP)
Trial / Age	Phase III / 60-80 y	Phase II / >80y	Phase II / 80 y
PS 0-1 %	78	66	70
Ann Arbor I-II %	36	25	23
aalPI 0-1 %	40	34	43
LDH > N %	65	68	57

- Taux de réponse identique

# Hétérogénéité pharmacologique

- Pharmacocinétique
  - Absorption
  - Distribution
    - protéines
  - Métabolisation
    - Perfusion hépatique, Cytochrome P450
  - Élimination
    - Rein
- compliance et polymédication
- Toxicité Spécifique

# Hétérogénéité Pronostique

## Prognostic factors for mortality

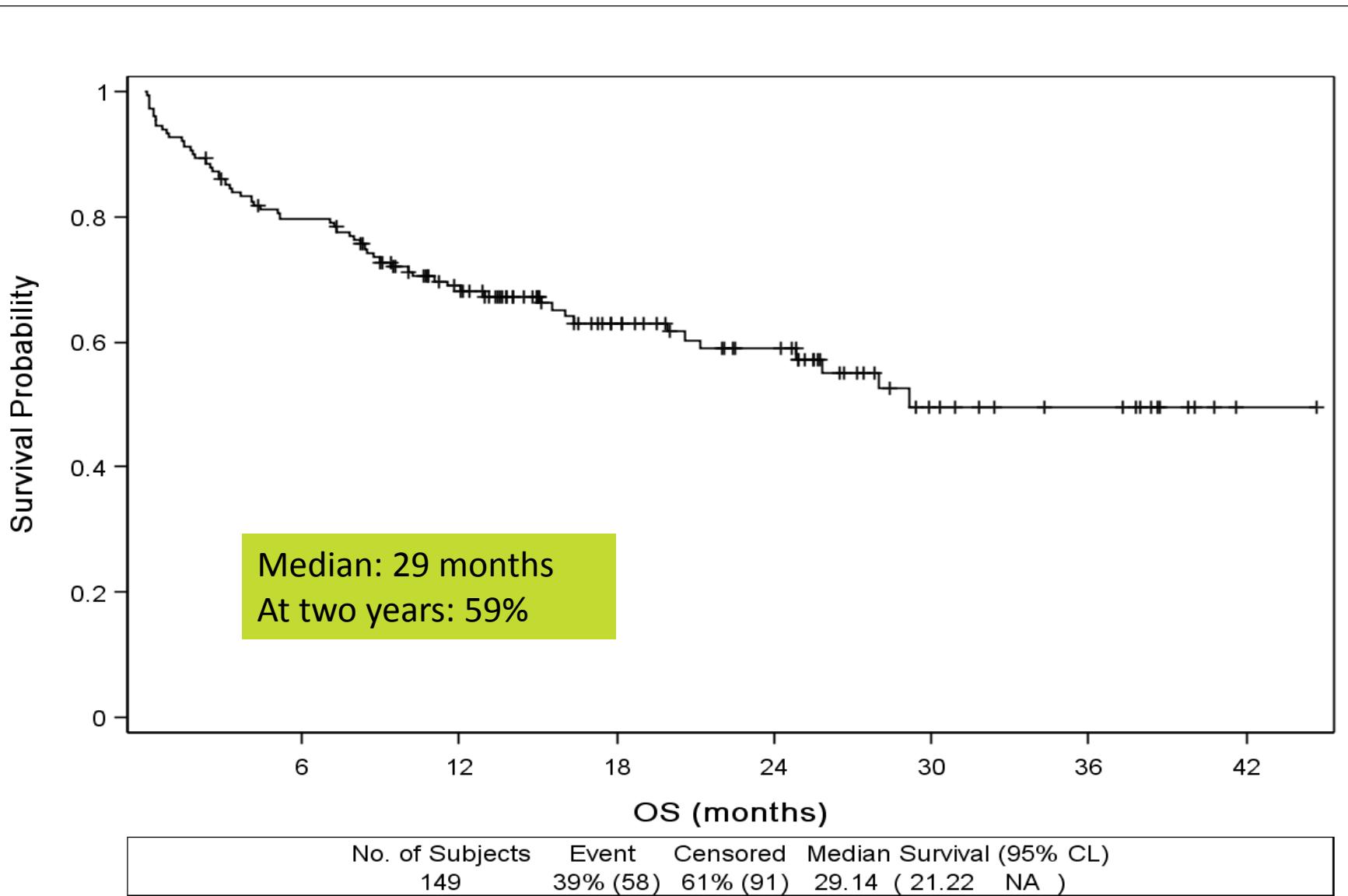
### Hematological malignancies in the elderly

	Study			Results univariate analyses								Results multivariate analyses										
	Author	Year of publication	Number of patients	Type of malignancy	Age	Performance status	Comorbidity	ADL	IADL	Cognition	Mood	Objective physical capacity	Nutritional status	Age	Performance status	Comorbidity	ADL	IADL	Cognition	Mood	Objective physical capacity	Nutritional status
Haematological malignancies only	Klepin	2013 (2011)	74	AML	-	-	-	-	-	+	-	+		-	-	-	-	+	-	+		
	Deschler	2013	195	AML/MDS	-	+	+	+	+	+	-*	+		-	+	+	+	-	-	-*	-	
	Corsetti	2011	21	AML/RAEB					-													
	Tucci	2009	84	DLBCL																		
	Soubeyran	2011	32	Non-Hodgkin lymphoma				+	+	+	+											
	Winkelmann	2011	143	Non-Hodgkin lymphoma	+	+	+	+	+					-	-	+	-	+				
	Rollot-Tard	2008	54	Various	+	+		+	+	+		(+)	-	-		-	-	-		(+)		
Various malignancies	Soubeyran	2012	348	Various	-	+	-	-	-	+	-	+	+	-	-	-	-	-	-	-	+	
	Wedding	2007	427	Various	+	+	+	-	+				+	+	+	-	-					
	Wildes	2013	65	Various	+	-	-	-	-	-	-	+	(-)	-	-	-	-	-	-	+	(-)	
	Proportion of studies with a significant association (%)				57	71	50	50	55	83	20	100	67	14	29	50	14	14	20	0	75	67

Based on a systematic Medline and Embase search, June 21<sup>st</sup> 2013

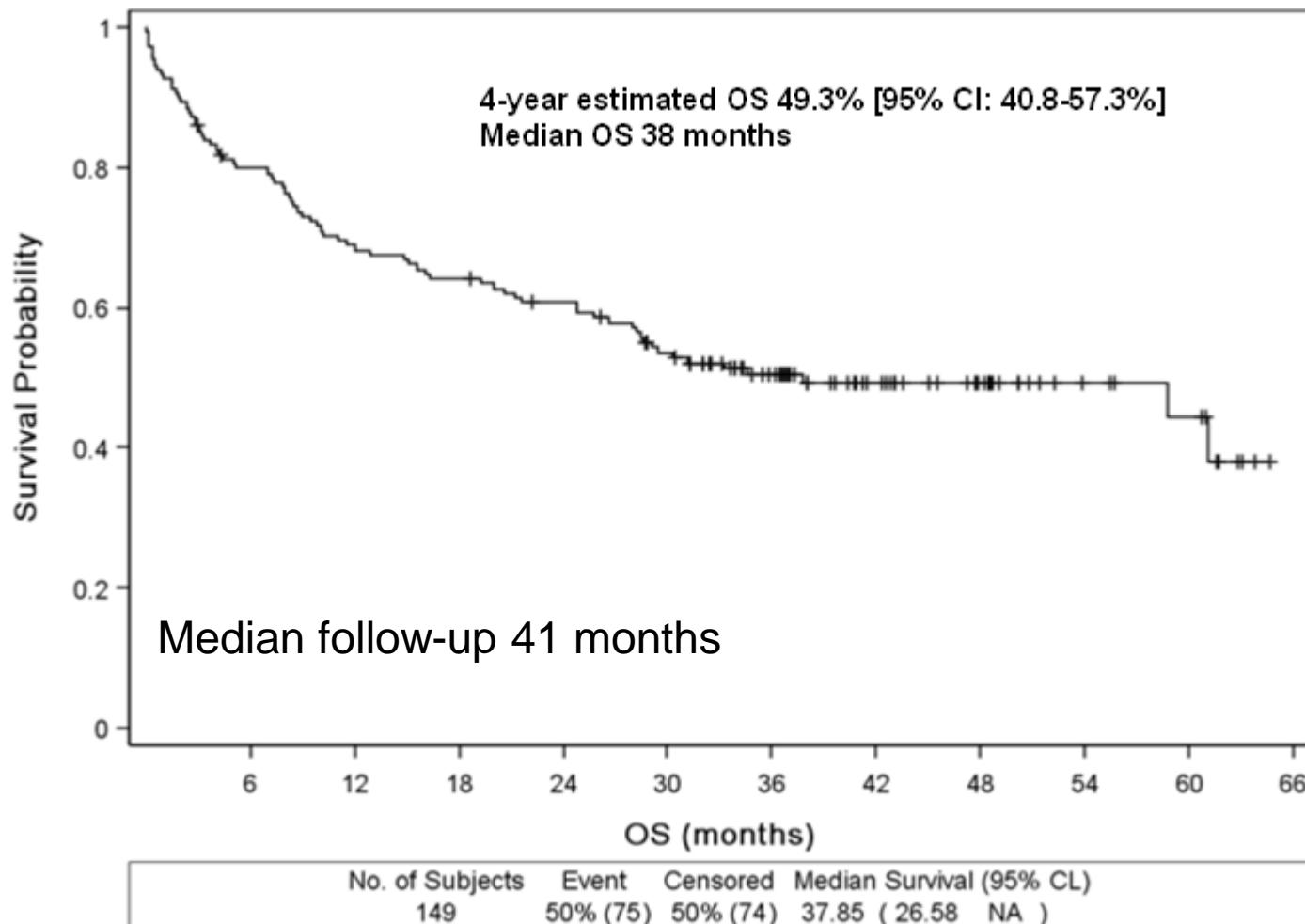
Hamaker M. et al, Leuk Res, 2014

# Survie Globale du R mini CHOP (>80 ans)



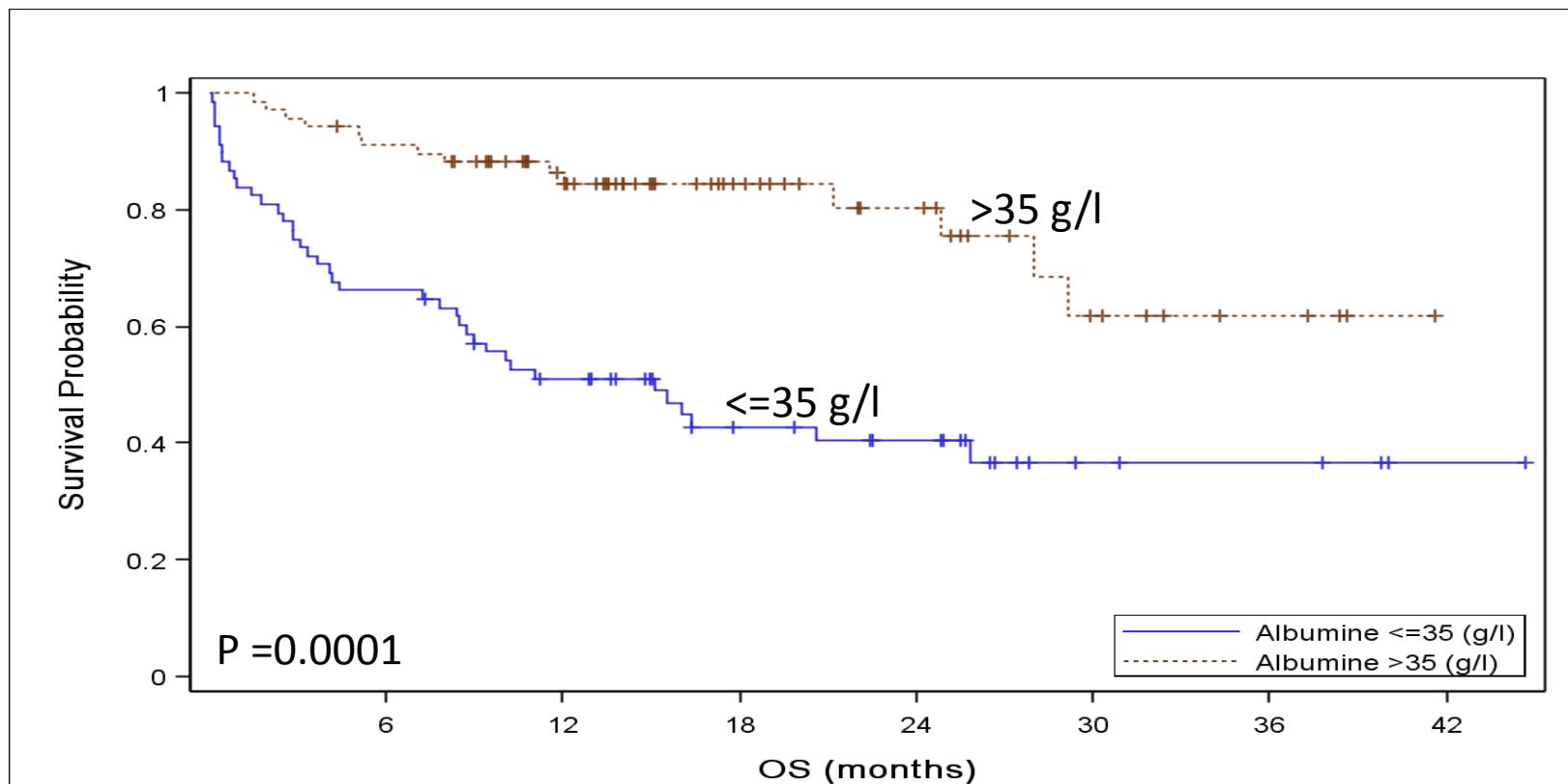
# Survie Globale du R mini CHOP (>80 ans)

## Suivi long terme



# Analyse Multivariée

## Taux d'albumine



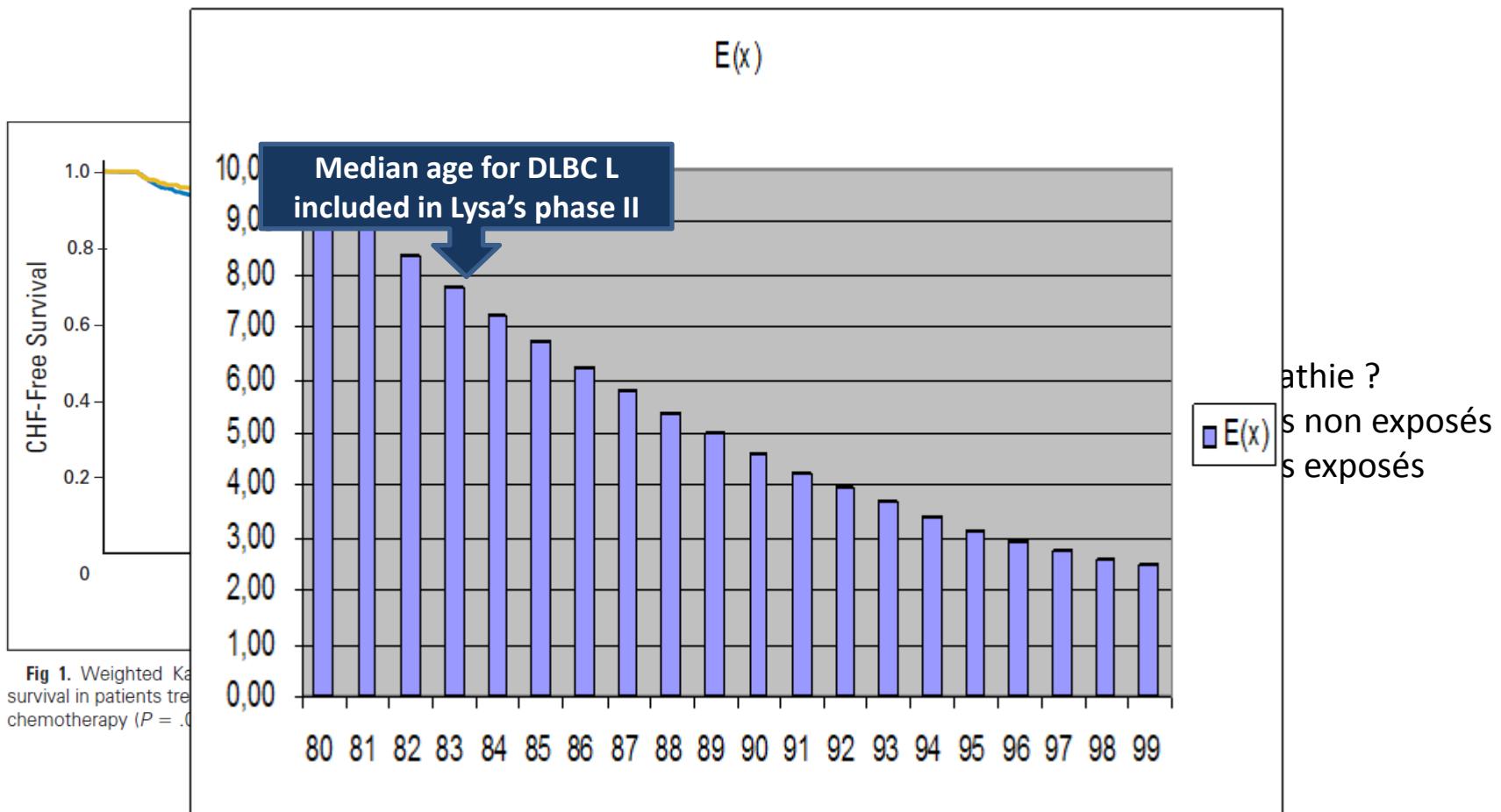
Albumine était le seul facteur pronostic de survie en analyse multivariée

# Causes de Décès

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	Toxicity	Lymphoma progression		Others	Total
Treatment Period	12 <i>(including 5 during the first cycle)</i>	8	7	1 bleeding 2 chest pain 1 poor general condition 1 pneumopathy 2 unknown causes	27
Follow-up Period	0	25	6	1 stroke 1 acute renal insufficiency 1 poor general condition 3 unknown	31
Total	12	33		13	58

Cumulative dose (mg/m <sup>2</sup> )	Probability of heart failure (%)			
	Every weeks		Every 3 weeks	
	40–59 years old	>60 years old	40–59 years old	>60 years old
7B trials: 150mg/m <sup>2</sup> ?	??	??	??	??
250	0.4	0.6	1.5	2.4
300	0.6	0.9	2.2	3.4
400	0.7	1.2	2.3	4.6
500	1.5	2.3	5.8	8.9
600	3.9	6.1	14.9	22.4
700	8.7	13.2	30.5	43.5



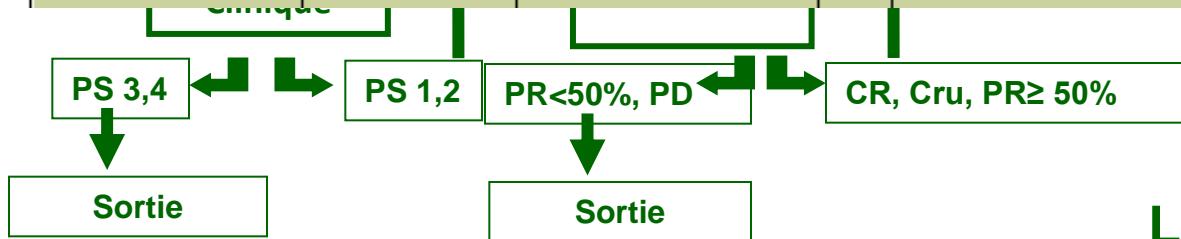
# 09-7B

PRE-PHASE

PHASE INDUCTION

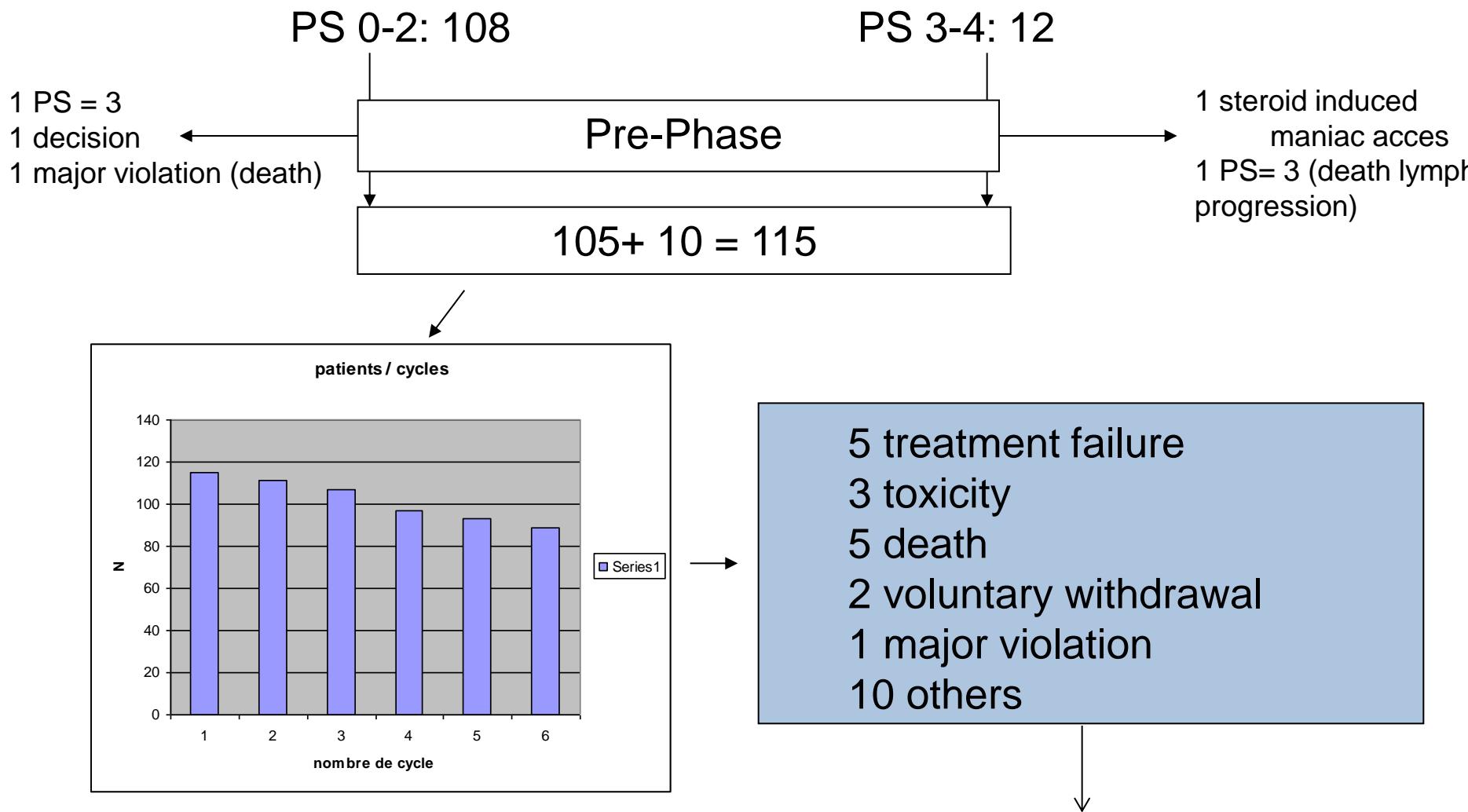
PHASE CONSOLIDATION

	Toxicity	Lymphoma progression	Others	Total
Treatment Period	12 <i>(including 5 during the first cycle)</i>	8	7 1 bleeding 2 chest pain 1 poor general condition 1 pneumopathy 2 unknown causes	27



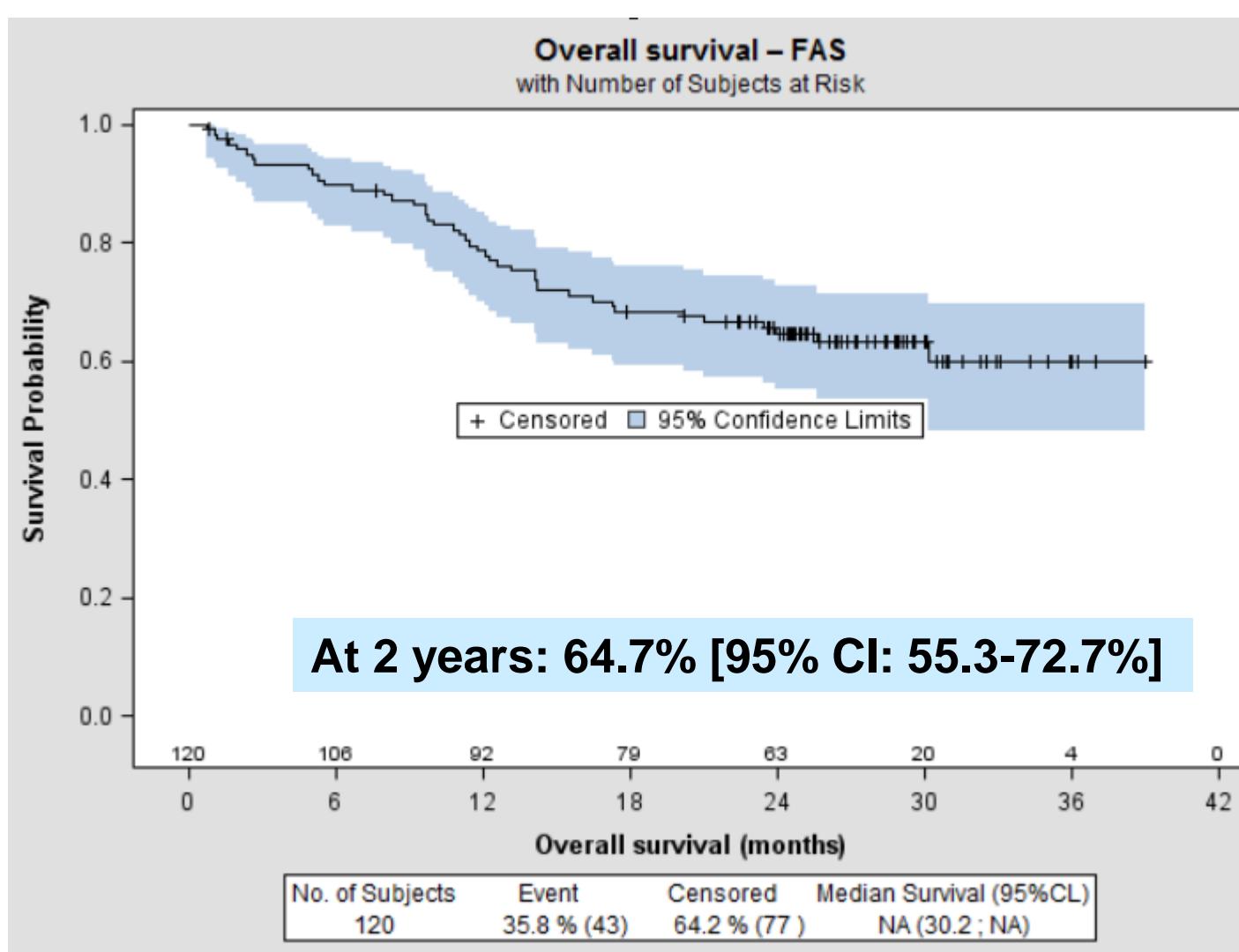
LNH 09-7B  
OmCHOP

**120 patients (from june 2010 à to jan 2011) median age 84 years (min 79 max 95)**



## **Median follow-up: 26.6 months**

# Primary endpoint: Overall survival FAS



# Causes de Décès

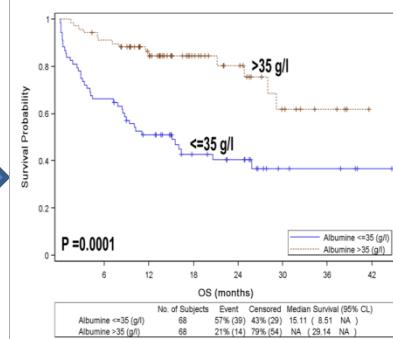
	Toxicity	Lymphoma progression	Others		Total
Treatment Period	0	3	3	1 pulmonary oedema 1 stroke 1 unknown causes	6
Follow-up Period	0	25	14	4 infectious diseases 4 psychiatric syndromes 3 unknown 2 cardiac failure 1 tractor accident	39
Total	0	28	17		45

# PROGNOSTIC FACTOR

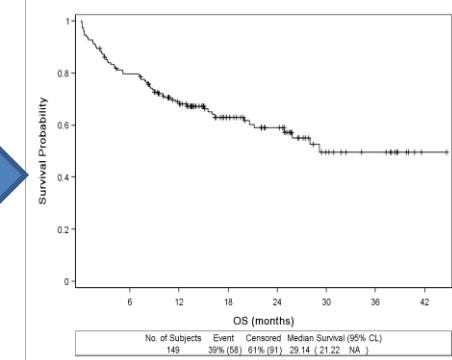
R-mini  
CHOP\*

	Toxicity	Lymphoma progression
Treatment Period	12 (including 5 during the first cycle)	8

Albuminaemia



OS at two years 59%

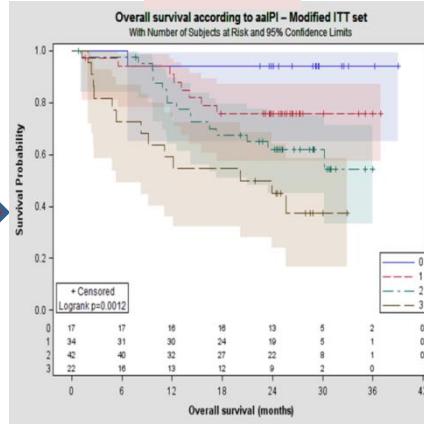


Pré-Phase

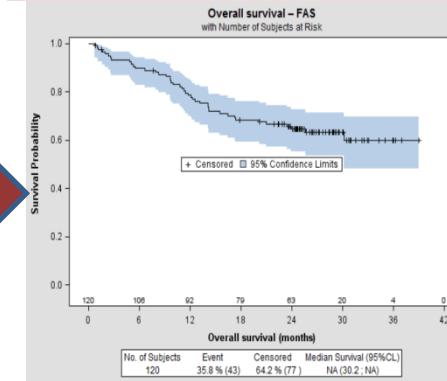
O-mini  
CHOP\*\*

	Toxicity	Lymphoma progression
Treatment Period	0	3

aalPI



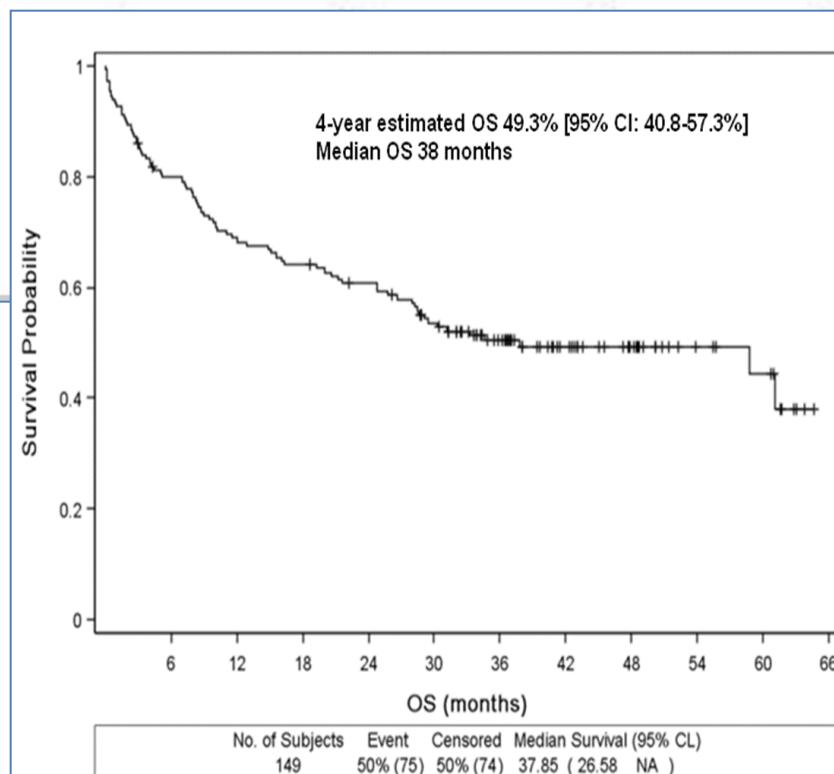
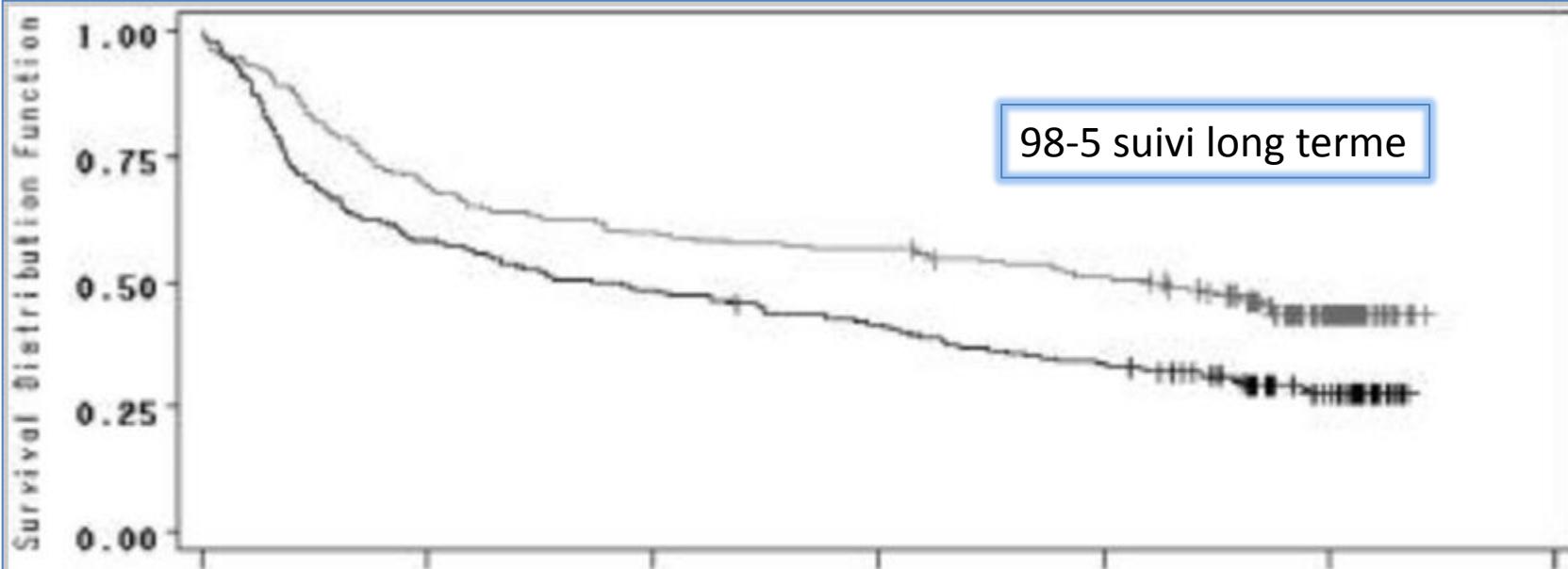
OS at two years 65%

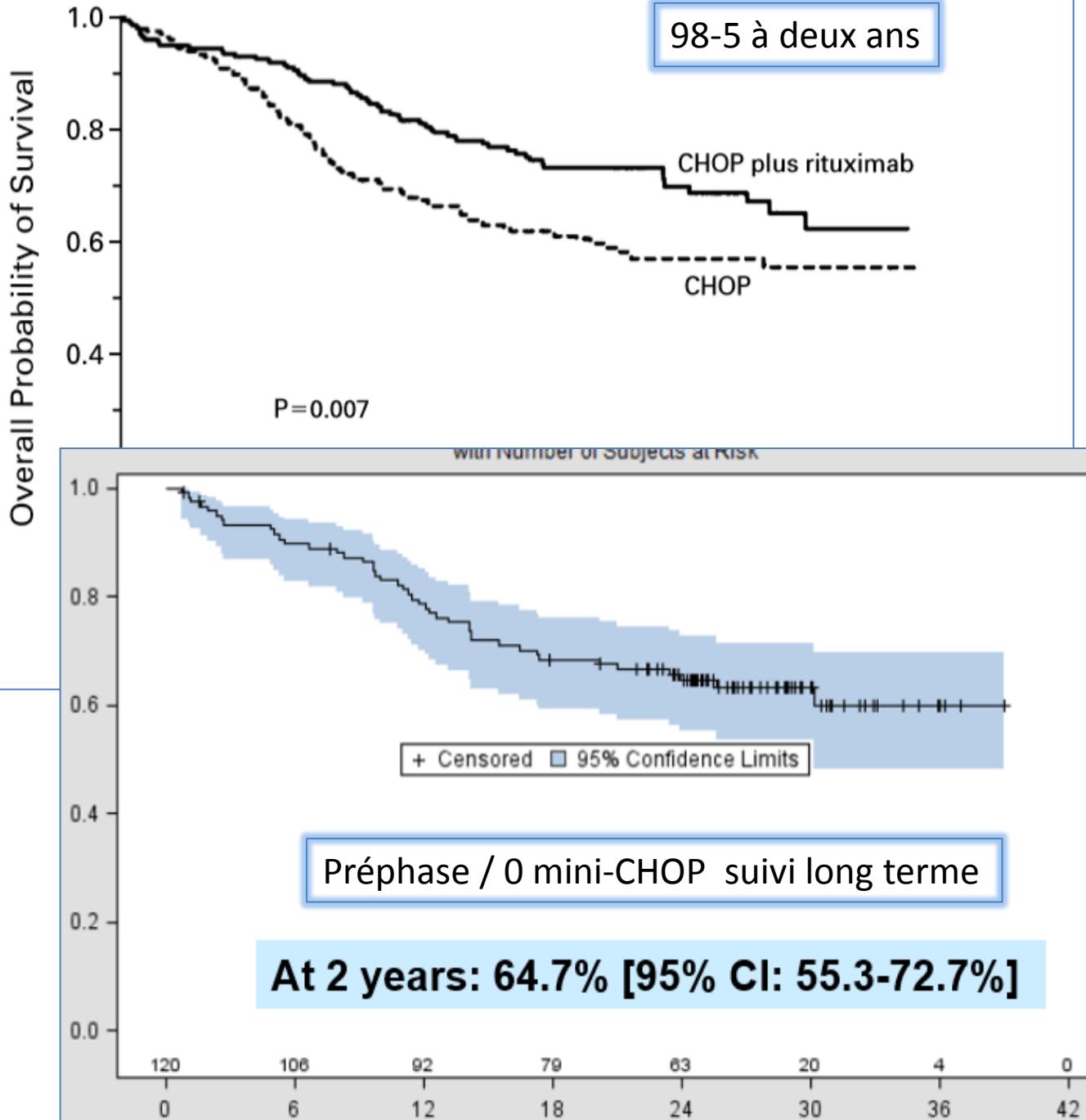


OS >80 y similar OS> 65 y

\*Peyrade F et al. Lancet Oncol. 2011;12(5):460–8

\*\*Peyrade F et al. Lancet Hematol 2017;4(1)





Le Lymphome du sujet âgé est donc un lymphome comme les autres.

Avec des besoins insatisfaits...

# Les besoins

- Phase I spécifique patients âgés

# Very few elderly patient in phase I studies

Table 1 Baseline patient characteristics, n = 233

Characteristic		Number	Median (range)
Gender	Male		
Age	Median (range)	57 (21-88)	
Performance status	ECOG 0		
	ECOG 1	122	52
	ECOG 2	6	3
No. of prior treatments			2 (0-14)
	0-2	135	58
	≥ 3	98	42
			46

Age at diagnosis, years

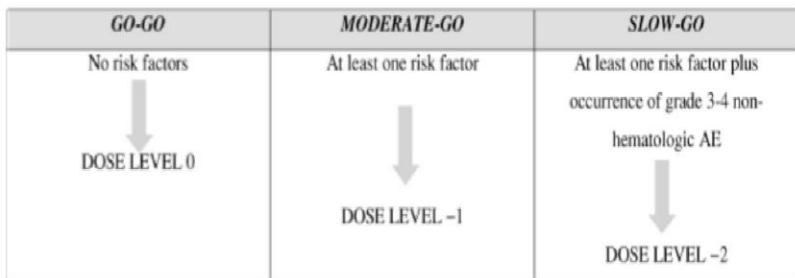
Median

52

Range	24–80	58.4	
Sex		3 (1-4)	
Male	104	58.0	9
Female	76	42.0	59
ECOG performance status			32
0	62	34.4	
1	116	64.4	
2	2	1.1	

Chau et al BMC Cancer 2011, 11:426  
Italiano et al Annals of Oncology 19: 787–792, 2008

Risk factors
• Age over 75 years
• Mild, moderate or severe frailty: patients needing help for household tasks and personal care*
• Comorbidities: cardiac dysfunction pulmonary dysfunction hepatic dysfunction renal dysfunction



Agent	DOSE LEVEL 0	DOSE LEVEL -1	DOSE LEVEL -2
Dexamethasone	40 mg/d d 1,8,15,22 / 4 wks	20 mg/d d 1,8,15,22 / 4 wks	10 mg/d d 1,8,15,22 / 4 wks
Melphalan	0.25 mg/kg or 9 mg/m <sup>2</sup> d 1-4 / 4-6 wks	0.18 mg/kg or 7.5 mg/m <sup>2</sup> d 1-4 / 4-6 wks	0.13 mg/kg or 5 mg/m <sup>2</sup> d 1-4 / 4-6 wks
Thalidomide	100 mg/d	50 mg/d	50 mg qod
Lenalidomide	25 mg/d d 1-21 / 4 wks	15 mg/d d 1-21 / 4 wks	10 mg/d d 1-21 / 4 wks
Bortezomib	1.3 mg/m <sup>2</sup> twice weekly d 1,4,8,11 / 3 wks	1.3 mg/m <sup>2</sup> once weekly d 1,8,15,22 / 5 wks	1.0 mg/m <sup>2</sup> once weekly d 1,8,15,22 / 5 wks
Prednisone	60 mg/m <sup>2</sup> d 1-4 or 50 mg qod	30 mg/m <sup>2</sup> d 1-4 or 25 mg qod	15 mg/m <sup>2</sup> d 1-4 or 12.5 mg qod
Cyclophosphamide	100 mg/d d 1-21 / 4 wks or 300 mg/m <sup>2</sup> /d d 1,8,15 / 4 wks	50 mg/d d 1-21 / 4 wks or 150 mg/m <sup>2</sup> /d d 1,8,15 / 4 wks	50 mg qod d 1-21 / 4 wks or 75 mg/m <sup>2</sup> /d d 1,8,15 / 4 wks

## PHASE I

- Richardson PG et al:  
Immunomodulatory drug CC-5013 ...  
Blood 100:3063-3067, 2002:  
**median age 65 ans**
- Zangari M et al: Results of phase I study of CC-5013... Blood 98:775a, 2001  
(abstr 3226):  
**median Age 62 ans**



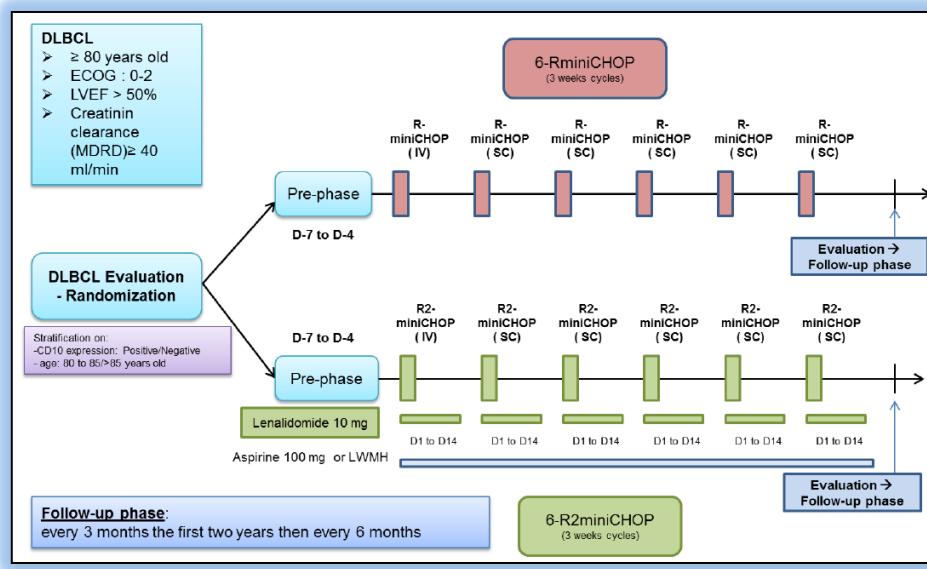
# Les Besoins

- Phase
- Phase
  - Très simple
  - 
  -



question  
h nodes after CT

- Phase III:
  - senior study: RminiCHOP +/- Lenalidomide



- CGA based clinical studies

# Phase IV

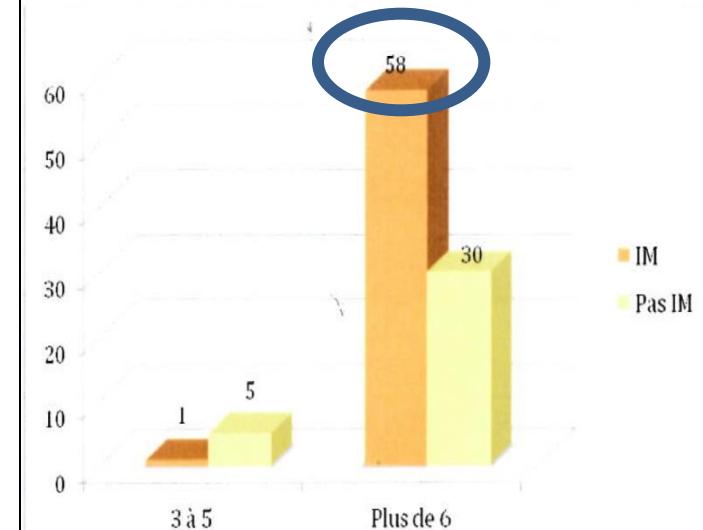
- Enquête vraie vie sur 100 patients > 65 ans traités pour un cancer
  - Compliance 50%
  - suivi ?
  - Interaction

Moyenne	EcartType	Min – Max
7.2	4.8	0 - 20

Nombre de molécules	Nombre de patients	Fréquence
Aucun	4	4.25%
1 à 2	10	10.64%
3 à 5	24	25.55%
Plus de 6	56	59.57%

: Relation nombre de molécules (protocole de TMAC inclus) - IM



Le Lymphome du sujet âgé est donc un lymphome comme les autres....insatisfait

Merci de votre attention