LCM: vers un changement de stratégie thérapeutique ?

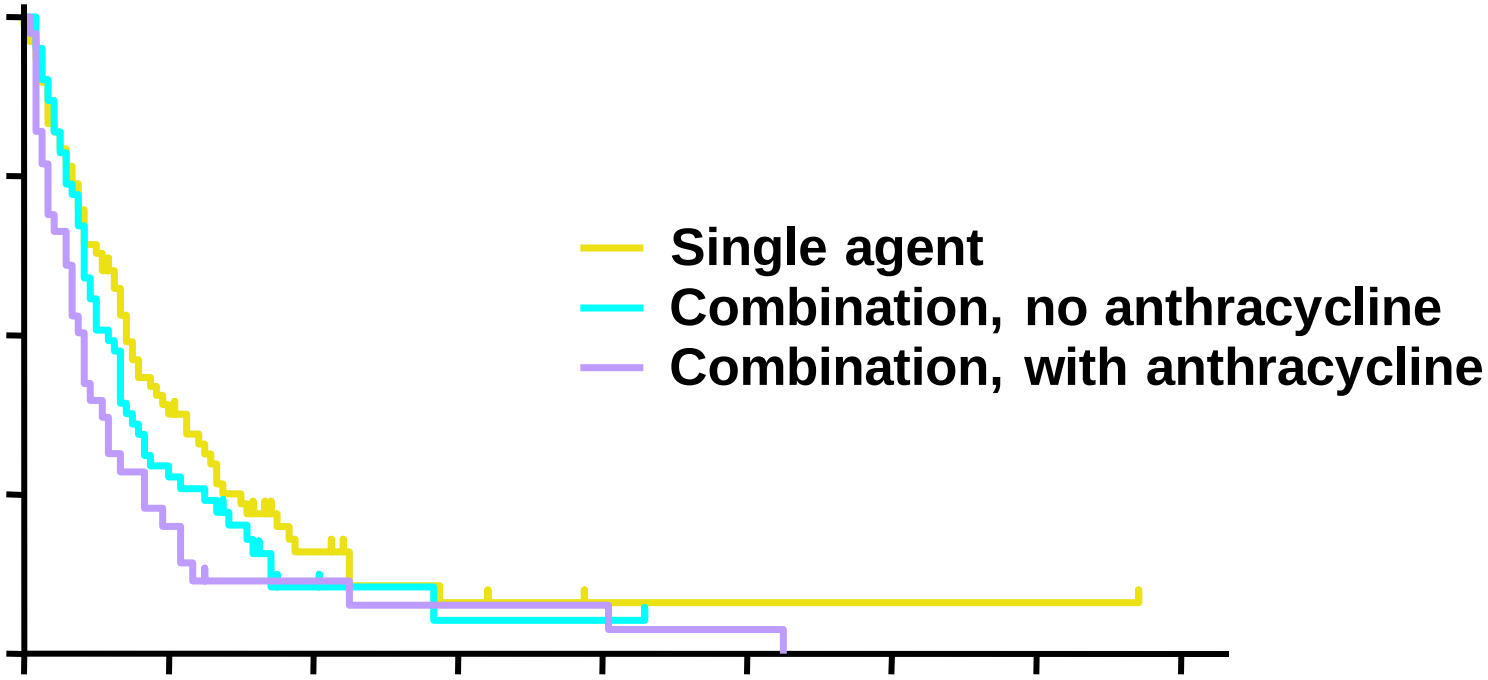
Prof. Le Gouill Steven
Université de Nantes
Service d'hématologie clinique
UMR 892 INSERM
Nantes
France

Efficacy of conventional chemotherapy II

Multicentre evaluation of MCL

Annecy Criteria fulfilled

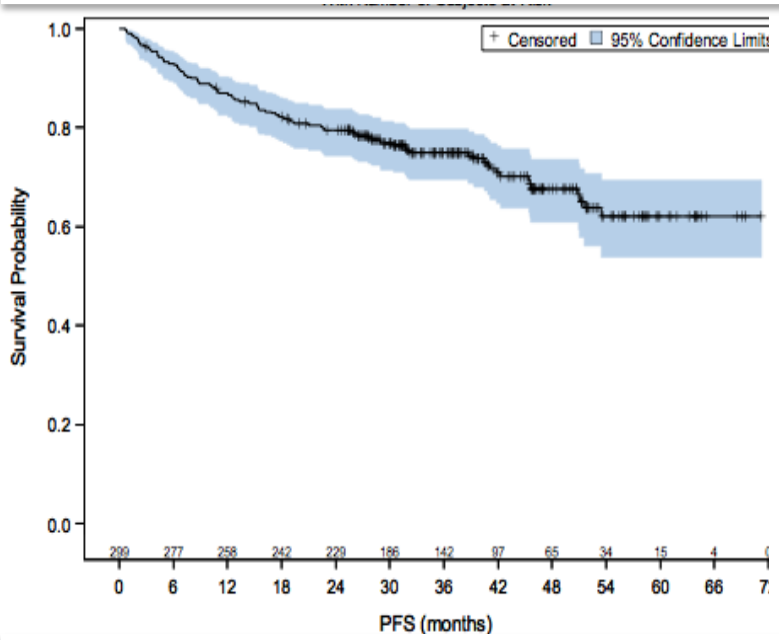
Event-free interval after chemotherapy in stages III + IV



Dreyling MH & Hiddemann W, *ASCO* 1999; Abstract 10.

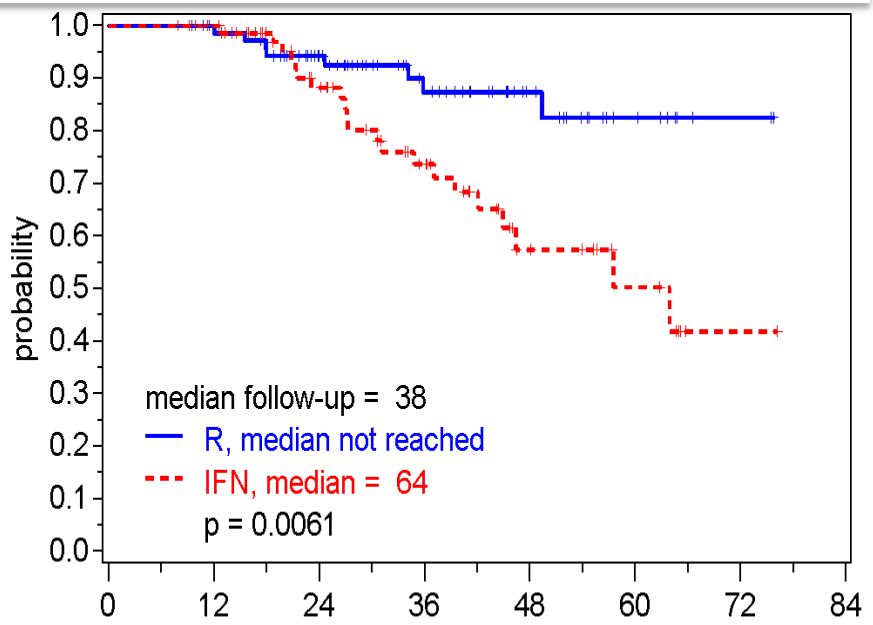
PFS of MCL patients is much more better than 10y ago

Young patients



Le Gouill et al. ASH 2014

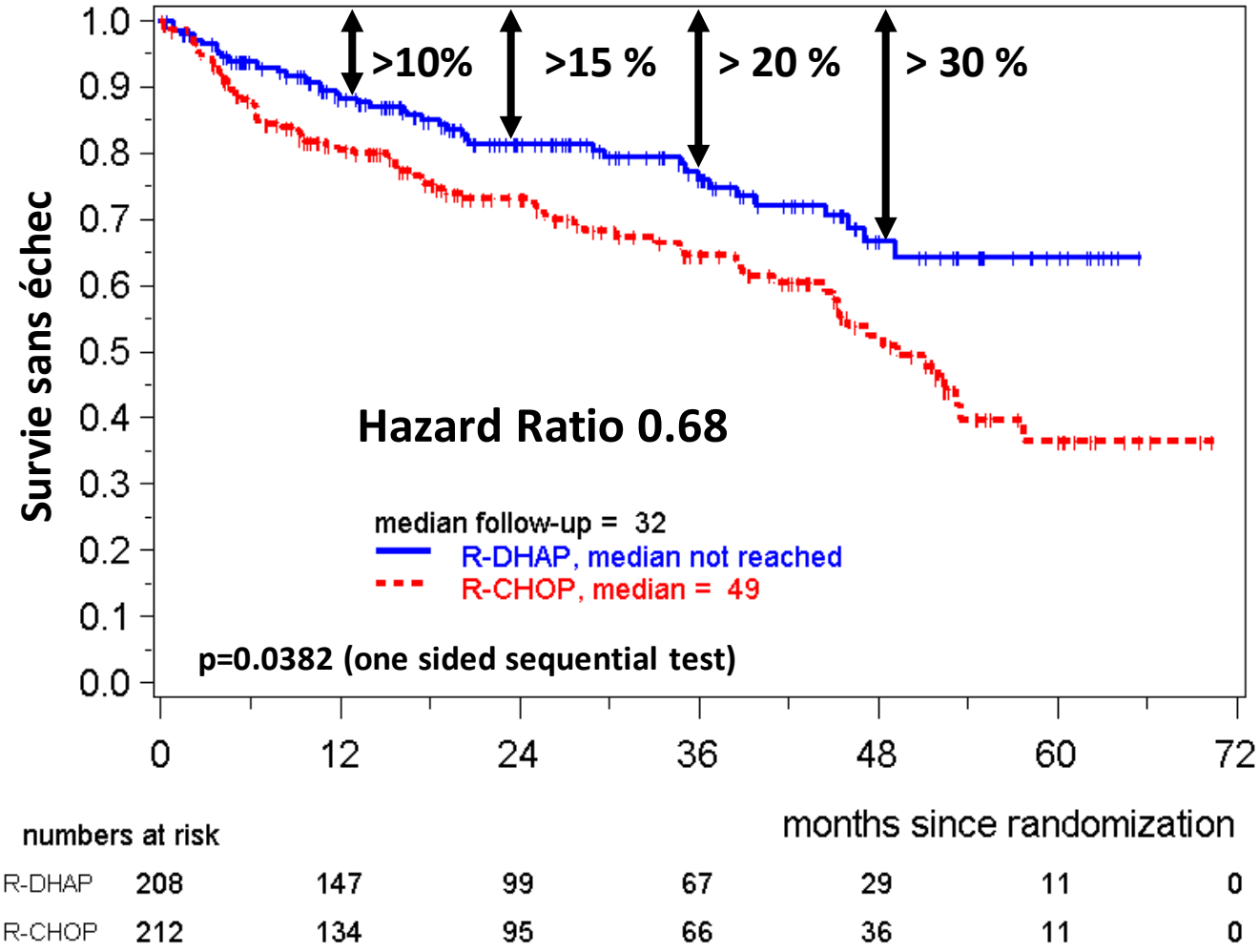
Elderly patients



Kluin-Nelemans NEJM

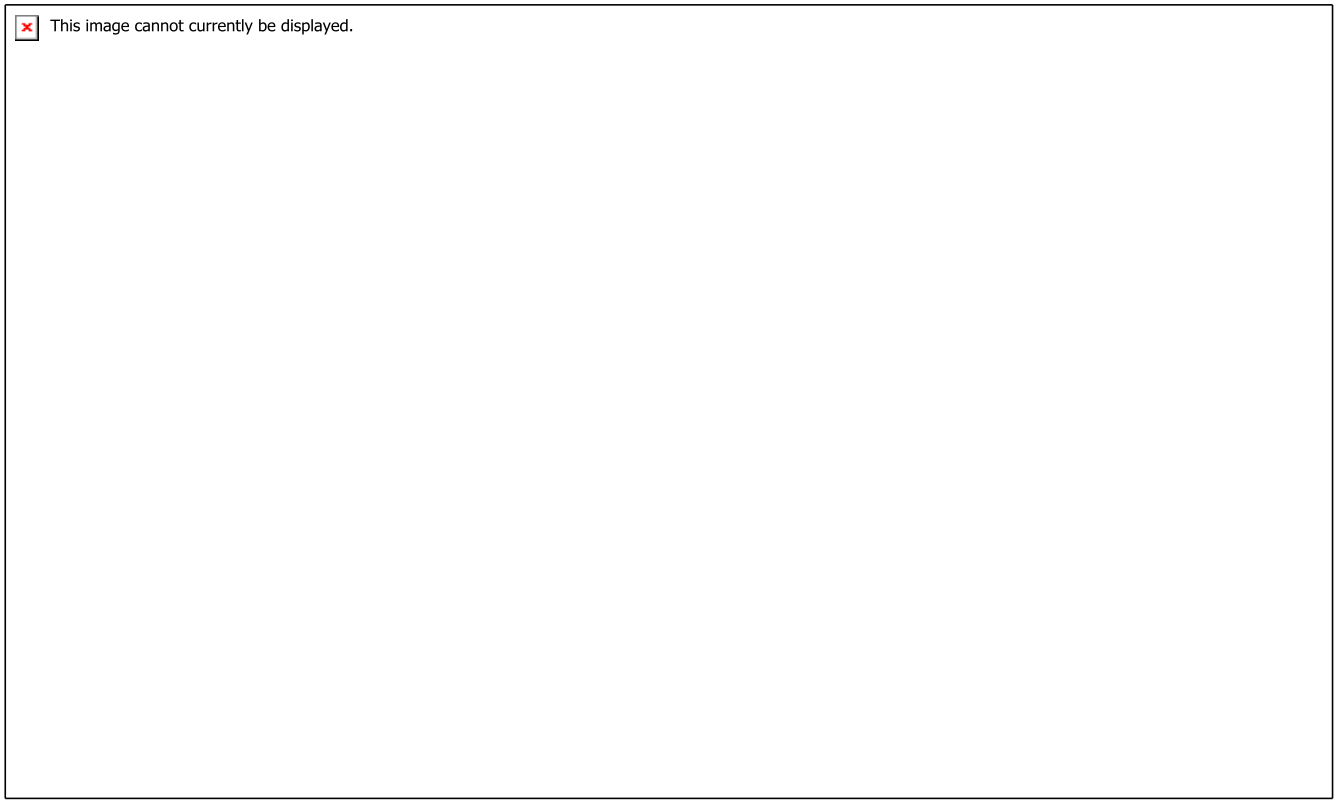
CONFIDENTIAL & PROPRIETARY -- NOT TO BE DISTRIBUTED.

Le LCM: exposé à la rechute



Adapté de Hermine, 2010

WE HAVE TO CHANGE BECAUSE MCL PATIENTS DO NOT LIVE IN CLINICAL TRIALS NOR IN GUIDELINES BUT IN REAL LIFE



NET OS in REAL life

Leux et al. Annals of Hematology 2014

Changer le traitement grâce à des nouvelles molécules

Treatment for R/R MCL

Treatment	Study or Literature Reference	N	ORR	CR	Median DOR (months)	Median PFS (months)	Median OS (months)
Ibrutinib	PCYC-1104-CA	111	68%	21%	17.5	13.9	Not reached
Bortezomib	Fischer 2006 Goy 2009	155[a]	33%	8%	9.2	6.5	23.5
Lenalidomide	Goy 2012	134	28%	8%	16.6	4.0	19.0
Temsirolimus[b]	Hess 2009	54	22%	2%	7.1	4.8	12.8

Campo & Rule Blood 2014

Ibrutinib: first in class but not alone in the class

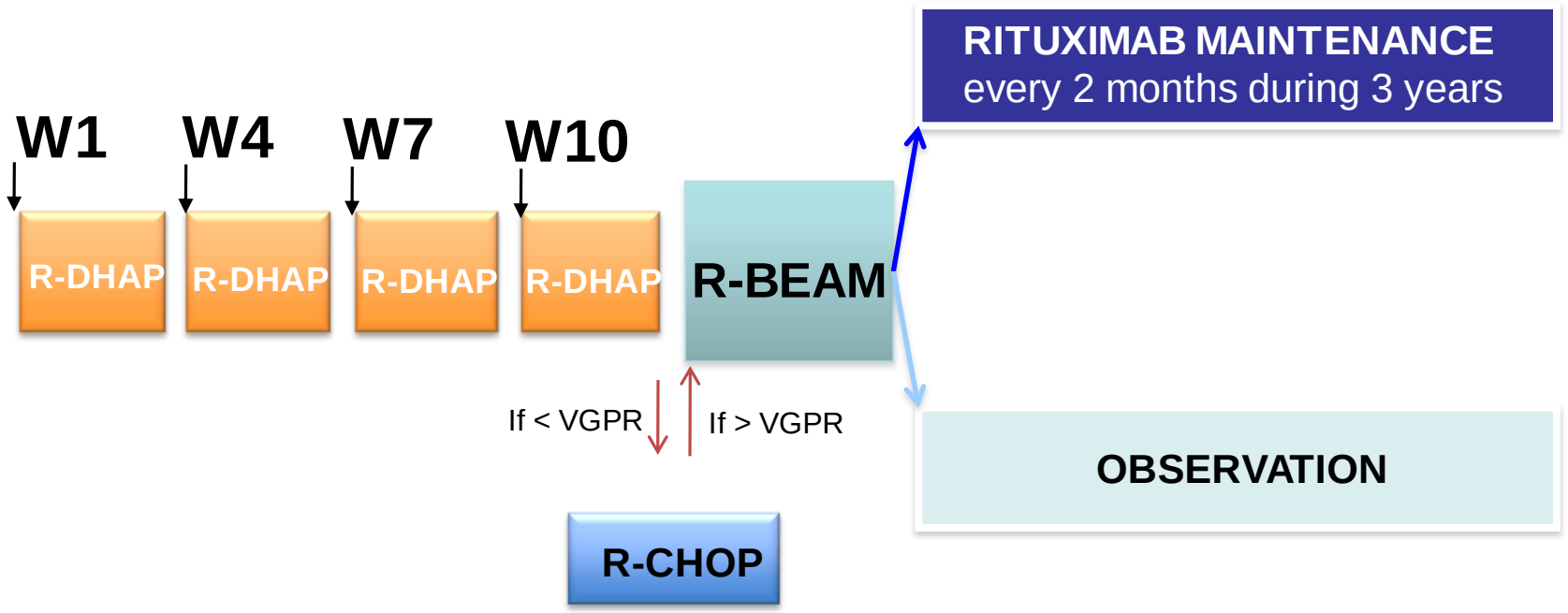
BTK	Pharma	disease	Clinical
IBRUTINIB	Parmacyclics/Janssen-Cilag	CLL and MCL	approved for clinical used
ONO-4059	ONO Pharmaceutical/Gilead	NHLs, CLL	Phase I
CC-292 (AVL 292)	Celgene	B-cell malignancies	Phase I
HM 71224	Hanmi	rheumatoid arthritis	FIH, healthy volonteers
ACP-196	Acerta	B-cell malignancies	FIH, phase I
BGB-3111	Beigene	B-cell malignancies	Phase I
CNX-774	Avila Therapeutics	?	preclinical
RN 486	F. Hoffmann-La Roche	autoimmune diseases	preclinical
GDC-0834	Genentech/Gilead	rheumatoid arthritis	preclinical
CGI 1746	CGI Pharmaceuticals	rheumatoid arthritis	preclinical
CGI 560	CGI Pharmaceuticals	rheumatoid arthritis	preclinical
LFM-A13	?	?	?

Agent	Phase	Number (evaluable) R/R MCL patients	Median no prior regimens (range)	ORR (CR+CRu)	Median PFS (months)	Median OS (months)	Reference
ABT-199	**1**	**6**	**3 (1–7)**	**100%**	**NR**	**NR**	**Davids 2012**
Cladribine		25 (24)	NR	46% (21%)	5.4	1.9	Inwards 2008
Clofarabine	1	6	1 (1–7)	67% (33%)	8	31	Abramson 2013
Deforolimus	2	9	3 (0–≥7)	33% (0%)	NR	NR	Rizzieri 2008
Everolimus	2	36 (35)	2 (1–3)	20% (6%)	5.5	NR	Renner 2012
Idelalisib	1	18 (16)	5 (1–12)	62% (0%)	NR	NR	Kahl 2010
Idelalisib	1	4 (3)	4 (1–13)	67% (0%)	NR	NR	Flinn 2012
IPI-145	2	15 (11)	4 (1–6)	27% (0%)	NR	NR	O'Connor 2008
Ixabepilone	2	16	3 (1–≥4)	36%	3.7	16.7	Churpek 2013
Ixabepilone	2	11	3 (1–≥5)	9% (9%)	3	10.5	Rolland 2010
MLN8237	2	9	2 (0–4)	0%	5.9	16.9	Kirschbaum 2011
Obinutuzumab	2	15	3 (1–17)	27% (13%)	2.65	9.8	Morschhauser 2013
Tipifarnib	2	13	3 (1–11)	23% (8%)	NR	NR	Friedberg 2011
Vorinostat		25 (24)	NR	46% (21%)	5.4	1.9	Inwards 2008

(NR = Not reported)

Changer la stratégie thérapeutique grâce à des nouveaux outils

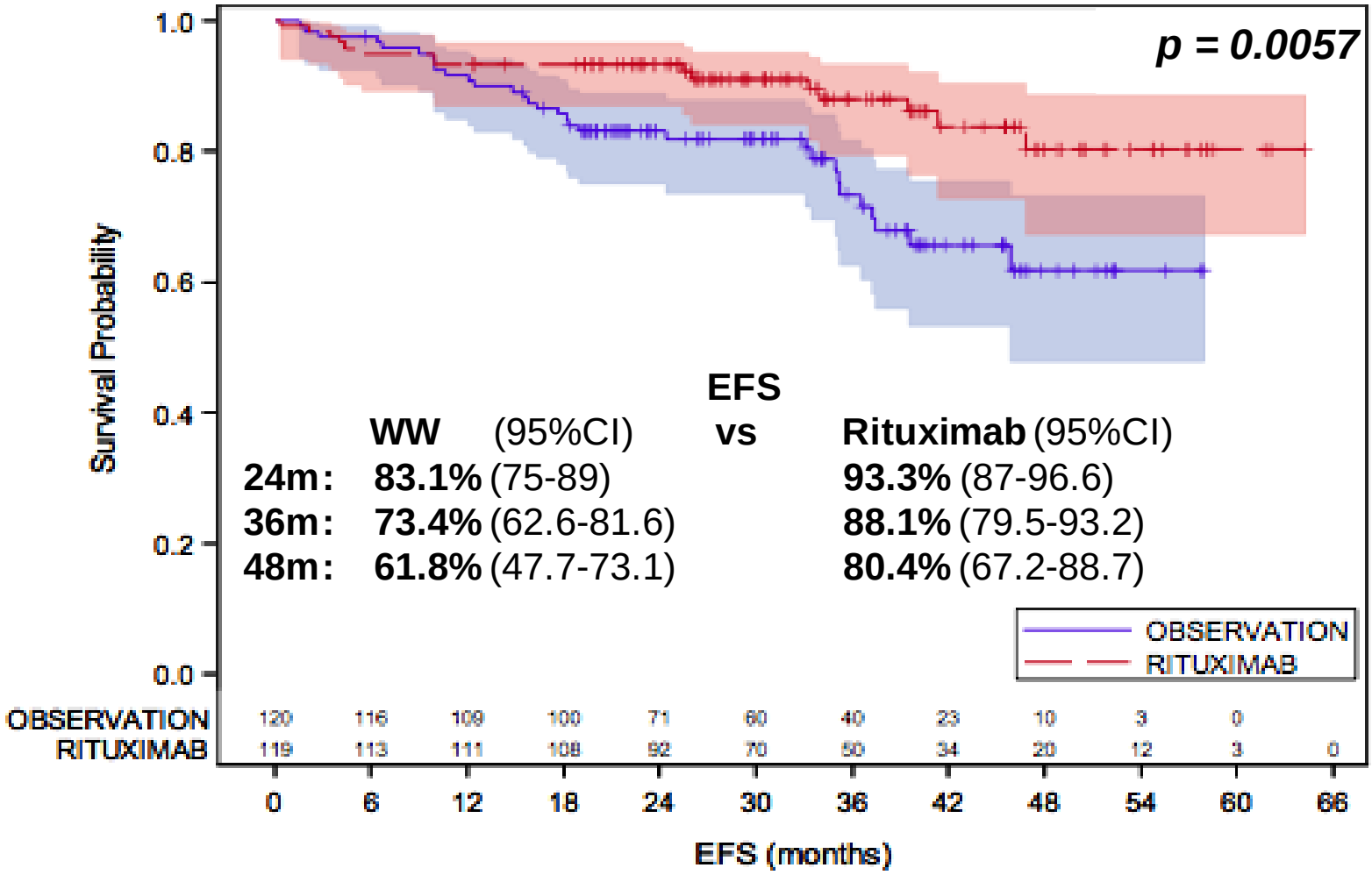
LyMa trial



R-DHAP: Rituximab 375mg/m2; aracytine 2g/m2 x2 IV 3 hours injection 12hours interval; dexamethasone 40mg d1-4; Cisplatin 100mg/m2 d1 (or oxaliplatin or carboplatin)

R-BEAM: Rituximab 500mg/m2 d-8; BCNU 300mg/m2 d-7; Etoposide 400mg/m2/d d-6 to -3; aracytine 400mg/m2/d d-6 to d-3; melphalan 140mg/m2 d-2

EFS from time of randomization



LyMa project

S. Le Gouill O. hermine	M. Callanan E Macintyre MH Delfau-Larue	C. Bodet-Milin M. Meignan	M. Maynadie	S. Minvielle	D. Canioni A. Moreau
LyMa Clinical trial	**LyMa MRD**	**LyMa FDG-TEP**	**LyMa Epidemiol.**	**LyMa Genomic**	**LyMa Envirron. Pathology**
Interim 2014 Final analysis 2016	Interim 2015 Final analysis 2017	Interim 2015 Final analysis 2017	Analysis 2016	Analysis 2016	Analysis 2017

Lysa
THE LYMPHOMA STUDY ASSOCIATION

Coordination: S. Le Gouill
Database LYSARC (S. Boussetta)
V. Rolland-Neyret (CP)

GOELAMS
Groupe Ouest-Est d'étude des Leucémies Aiguës et autres Maladies du Sang

LyMa project

S. Le Gouill O. hermine	M. Callanan E Macintyre MH Delfau-Larue	C. Bodet-Milin M. Meignan	M. Maynadie	S. Minvielle	D. Canioni A. Moreau
LyMa Clinical trial	LyMa MRD	**LyMa FDG-TEP**	LyMa Epidemiol.	LyMa Genomic	LyMa Envirron. Pathology
Interim 2014 Final analysis 2016	Interim 2015 Final analysis 2017	Interim 2015 Final analysis 2017	Analysis 2016	Analysis 2016	Analysis 2017

Coordination: S. Le Gouill
Database LYSARC (S. Boussetta)
V. Rolland-Neyret (CP)

Lysa
THE LYMPHOMA STUDY ASSOCIATION

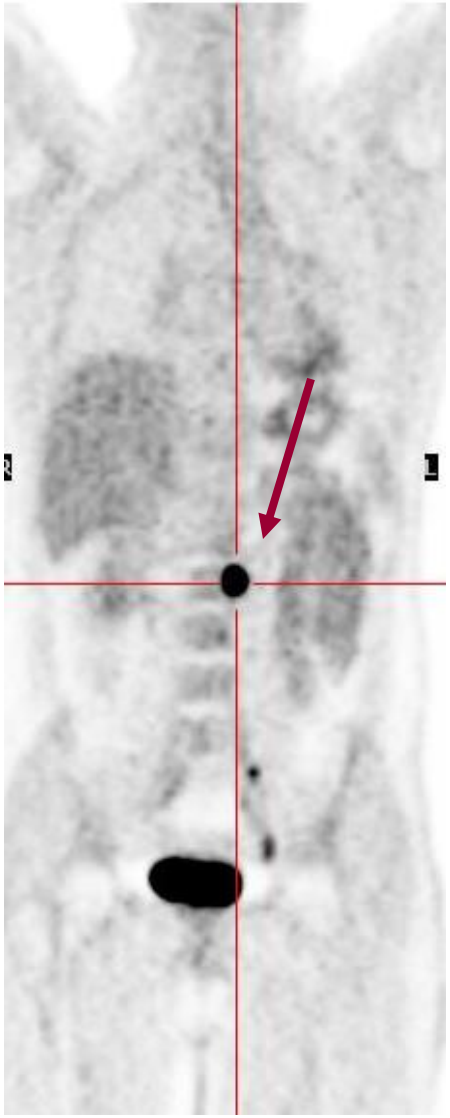
GOELAMS
Groupe Ouest-Est d'étude des Leucémies Aiguës et autres Maladies du Sang

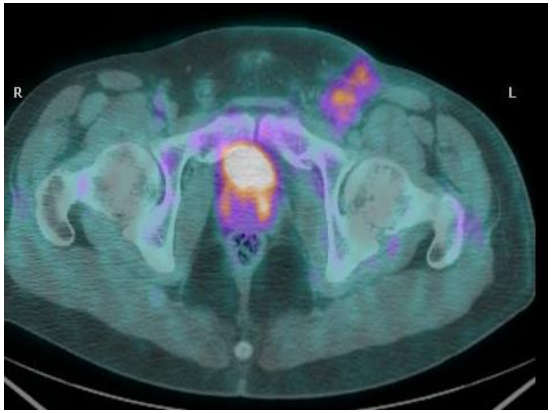
Predictive Power of FDG-PET Parameters at Diagnosis and after Induction in Patients with Mantle Cell Lymphoma, Interim Results from the LyMa-PET Project, Conducted on Behalf of the Lysa Group

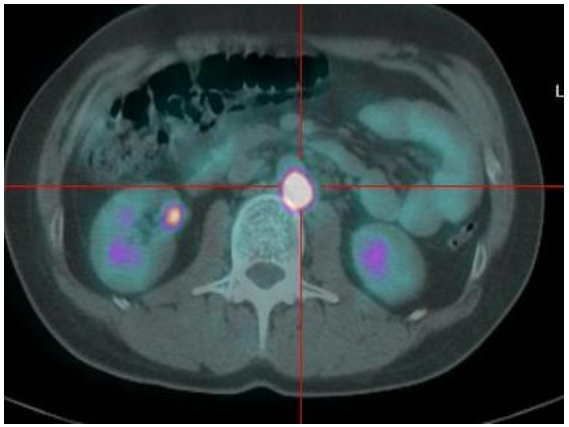
Caroline Bodet-Milin, Clement Bailly, Michel Meignan, Alina Beriollo-Riedinger, Rene-Olivier Casasnovas, Anne Devillers, Thierry Lamy, Maria Santiago-Ribeiro, Emmanuel Gyan, Céline Gallazzini-Crépin, Remy Gressin, MD, Thomas Carlier, Francoise Kraeber-Bodéré, Olivier Hermine, Steven Le Gouill

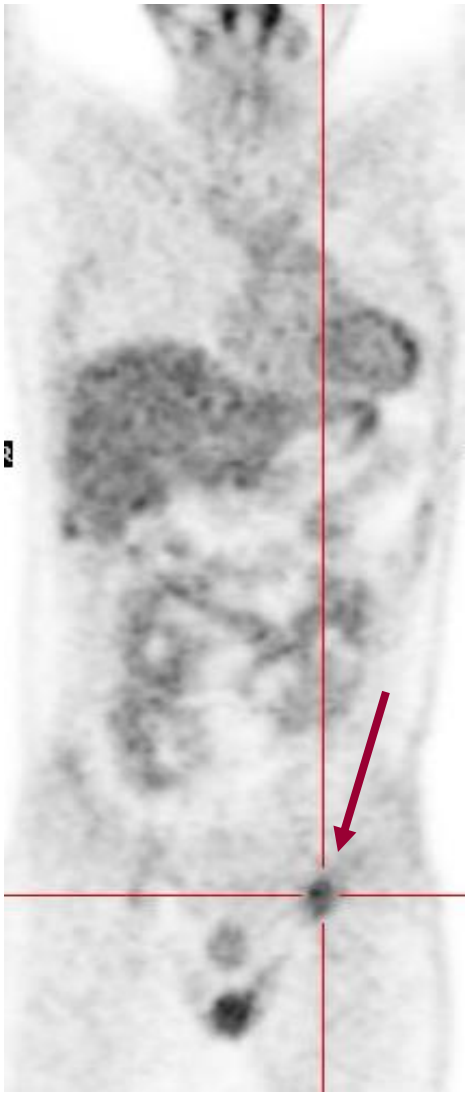
Lysa
THE LYMPHOMA STUDY ASSOCIATION

Orlando, ASH 2015 abstract 335



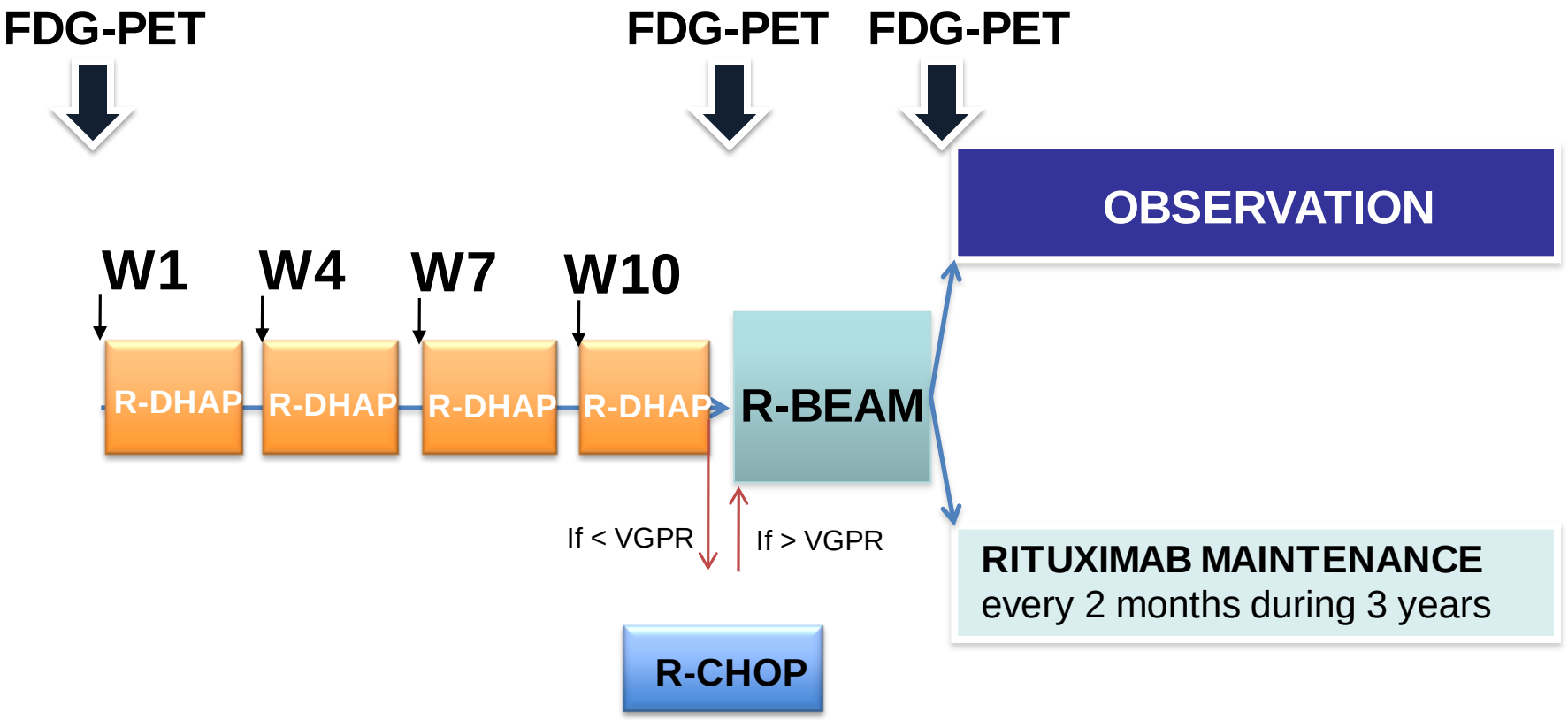






Bodet –Milin C. …. Le Gouill s. ASH 2015, Orlando

LyMa trial



R-DHAP: Rituximab 375mg/m2; aracytine 2g/m2 x2 IV 3 hours injection 12hours interval; dexamethasone 40mg d1-4; Cisplatin 100mg/m2 d1 (or oxaliplatin or carboplatin)

R-BEAM: Rituximab 500mg/m2 d-8; BCNU 300mg/m2 d-7; Etoposide 400mg/m2/d d-6 to -3; aracytine 400mg/m2/d d-6 to d-3; melphalan 140mg/m2 d-2

Results

94 untreated mantle cell lymphoma patients of the Lyma trial population (n=299)

No difference with LyMa population in terms of baseline characteristics, demographic data and staging.

2y-PFS from registration at 79.8 % vs 79.4% in LyMa population. (Interim analysis)

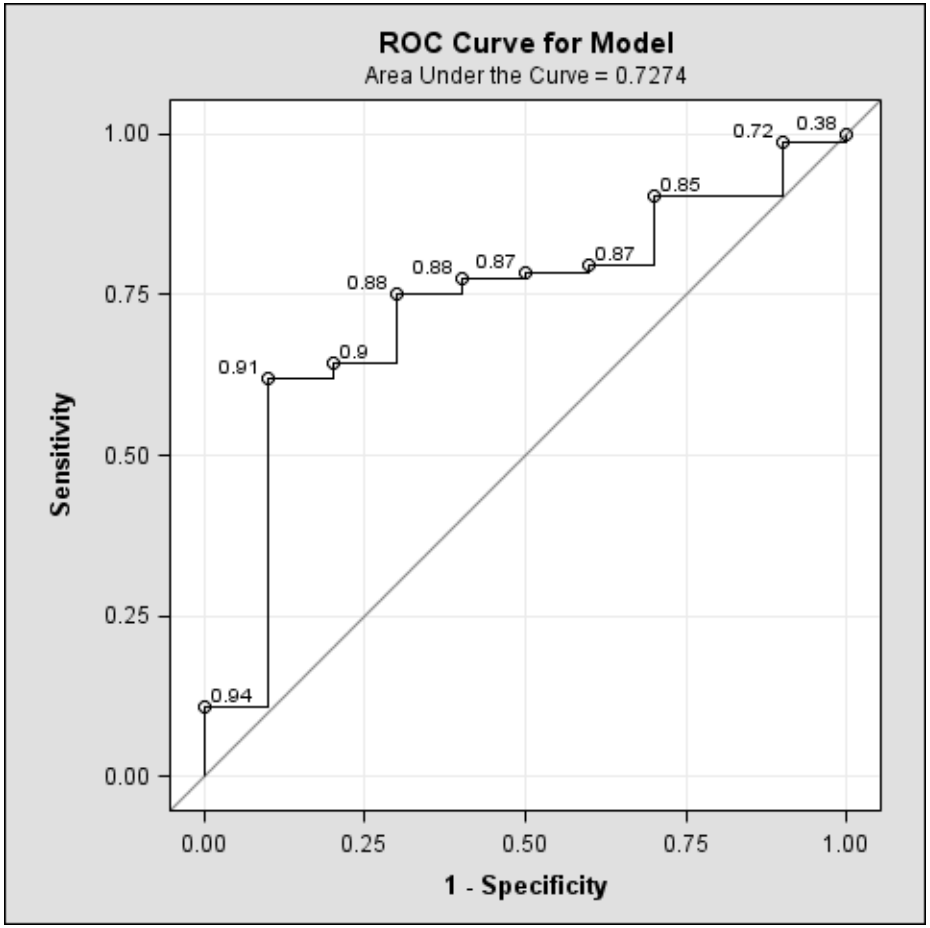
	LYMA-PET population (n=94)	LYMA population (n=299)
Age at inclusion (years)		
Mean (SD)	55,29 (6,51)	55,73 (6,71)
Median	56	57
Sexe		
Male	72 (76,6%)	236 (78,9%)
Female	22 (23,4%)	63 (21,1%)
Treatment arm		
Non-randomized	12 (12,8%)	60 (20,1%)
Observation	38 (40,4%)	125 (41,8%)
Rituximab	44 (46,8%)	114 (38,1%)
Staging		
Stage 1-2	4 (4,3%)	18 (6.0%)
Stage 3	16 (17%)	31 (10,4%)
Stage 4	74 (78,7%)	249 (83,6%)
Blastic variant	6 (9,7%)	12 (5,8%)
MCL International Prognostic Index (MIPI)		
Low	51 (54,3%)	159 (53,2%)
Int	28 (29,8%)	82 (27,4%)
High	15 (16%)	58 (19,4%)

Prognostic value of FDG-PET parameters at time of diagnosis

Parameters	PFS		OS	
	Threshold	p-value	Threshold	p-value
SUVmax	**11.4**	**<0.001**	**10.5**	**<0.001**
SUVmean	**7.7**	**<0.001**	**5.9**	**<0.001**
SUVpeak	**8.7**	**<0.001**	**8.7**	**<0.001**
Volume	25.5	0.005	27.7	0.095
TLG	126.4	0.012	2167	0.016

Prognostic value of FDG-PET parameters at time of diagnosis

ROC analysis of SUVmax on Blastoid form prediction



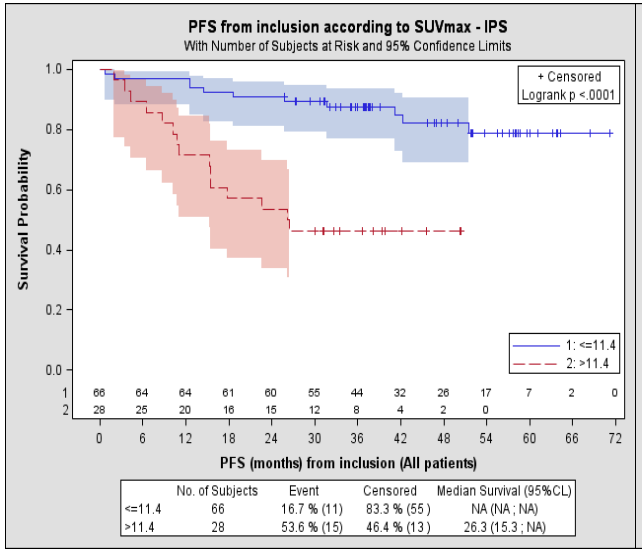
Best cut off at 7,3

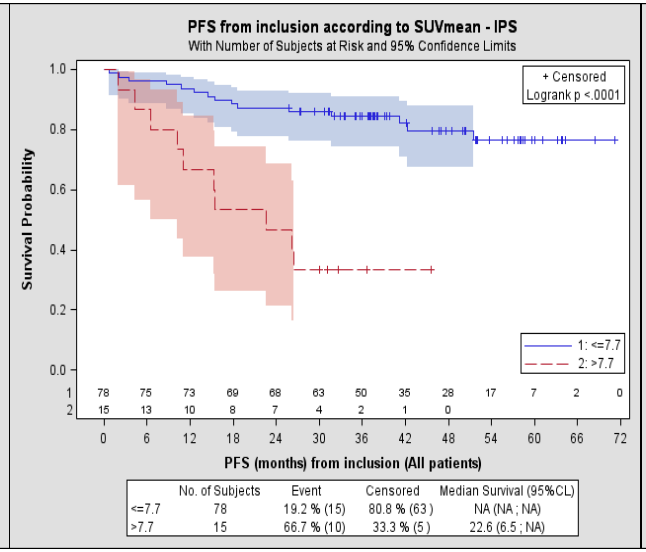
- **Se 62%**
- **Spe 90%**

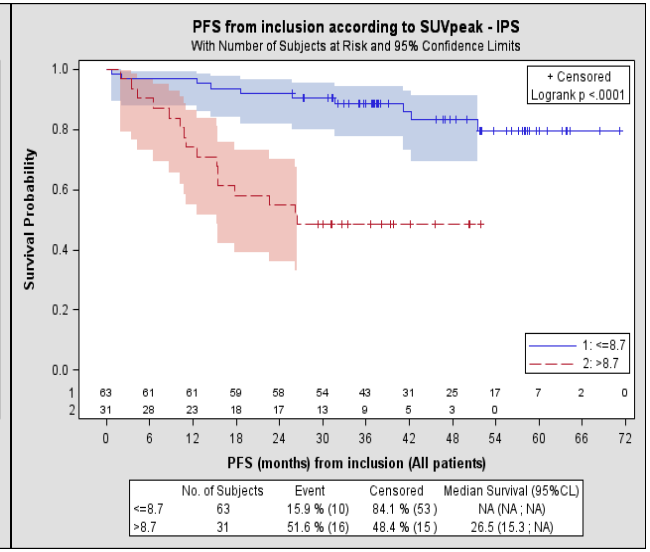
Prognostic value of FDG-PET parameters at time of diagnosis

Univariate analysis showed a strong prognostic value on **PFS of 3 metrics**:

SUV_{max} (p<0.001, cutoff=11.4)	SUV_{mean} (p<0.001, cutoff=7.7)	SUV_{peak} (p<0.001, cutoff=8.7)





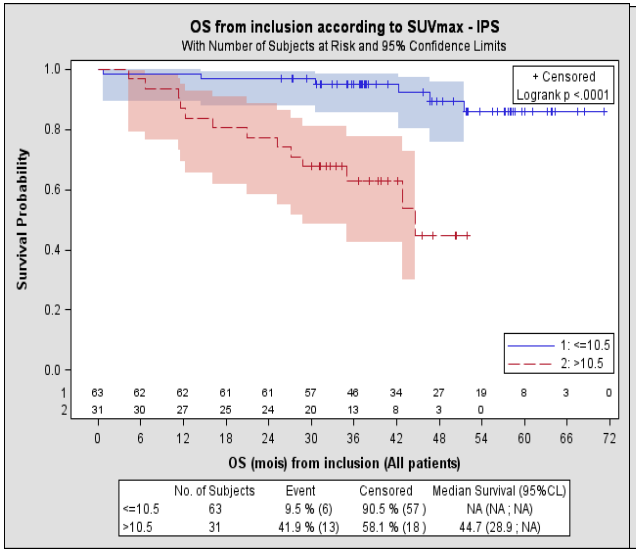


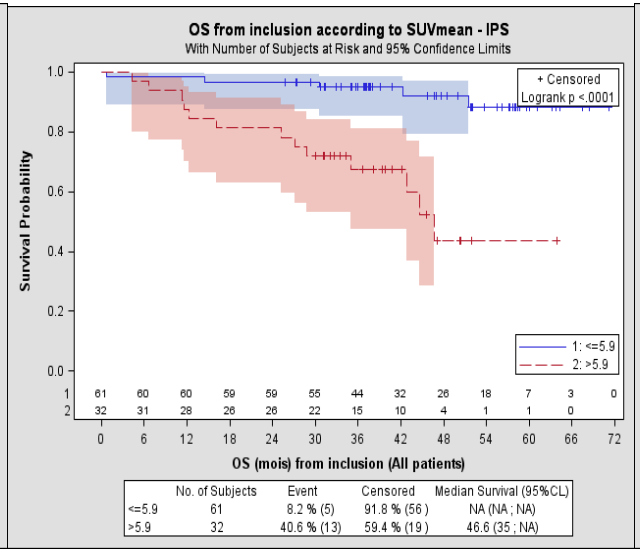
PARAMETER	Modality test	HR	IC-95%	*P*
SUVmax	>11.4	5.979	2.6-13.7	***< 0.0001***
MIPI	high	1.881	0.59-6.02	*0.287*
(low, ref)	intermediate	2.486	1.057-5.848	*0.0369*

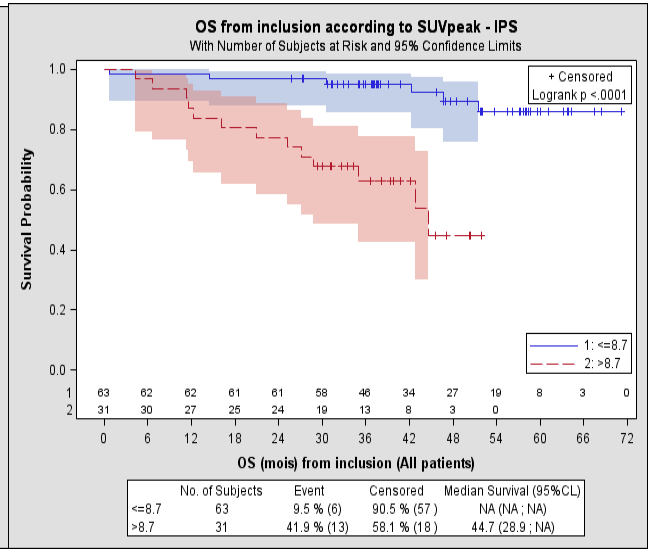
Prognostic value of FDG-PET parameters at time of diagnosis

Univariate analysis showed a strong prognostic value **on OS of 3 metrics**:

SUV_{max} (p<0.001, cutoff=10.5)	SUV_{mean} (p<0.001, cutoff=5.9)	SUV_{peak} (p<0.001, cutoff=8.7)



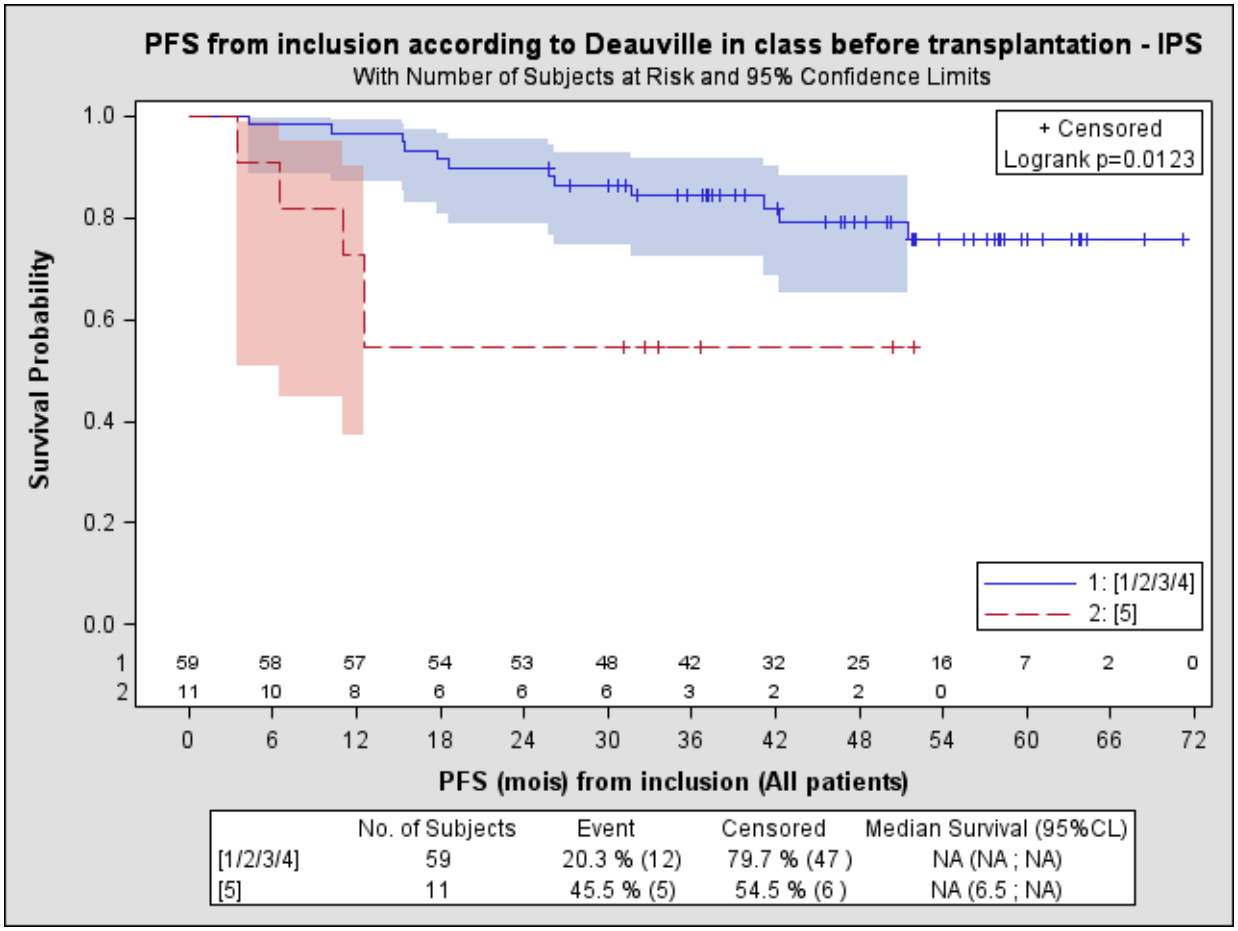




Prognostic value of ΔSUV parameters at the end of induction

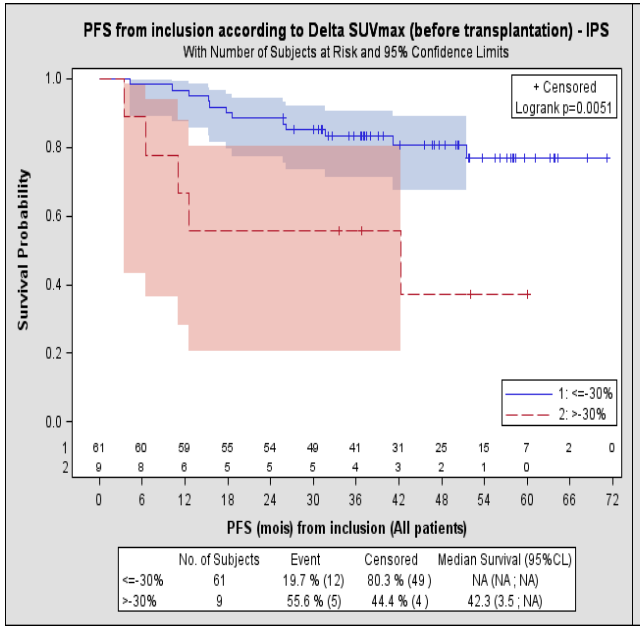
Parameters	PFS		OS	
	Threshold	p-value	Threshold	p-value
ΔSUVmax	**-30%**	**0.005**	**-39%**	**0.005**
ΔSUVpeak	**-41%**	**0.003**	**-41%**	**0.003**
ΔSUVmean	**-20%**	**0.0006**	**-32%**	**0.001**
Cheson		<0.001		0.374
Deauville (1/2/3/4 vs 5)		**0.012**		**0.013**

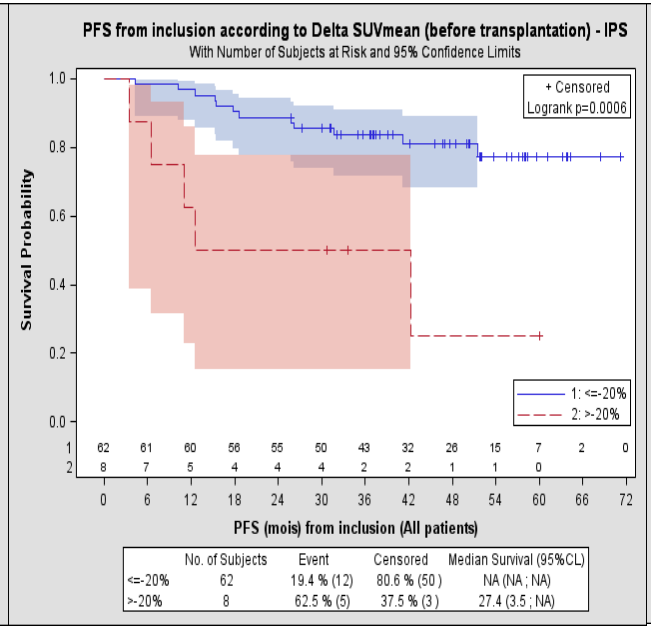
Prognostic value of ΔSUV parameters at the end of induction

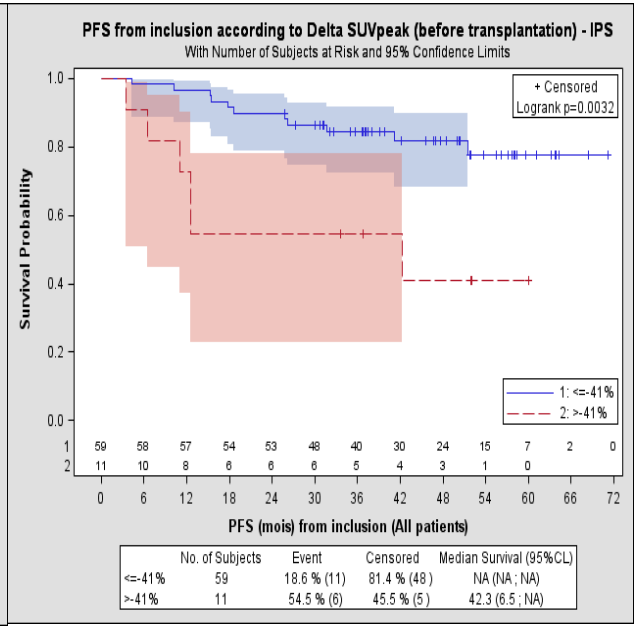


Prognostic value of ΔSUV parameters at the end of induction

ΔSUV_{max} (p=0.005, cutoff=-30%)	ΔSUV_{mean} (p=0.0006, cutoff=-20%)	ΔSUV_{peak} (p=0.003, cutoff=-41%)







- Correlation between SUVmax and Blastoid variant

- The present analysis performed from a group of patients homogeneously treated in a prospective trial shows for the first time that FDG-PET parameters at diagnosis like SUVmax (≤/>11.4), SUVmean or SUVpeak provide key parameters to predict PFS in MCL.

- ΔSUV parameters calculated from time of diagnosis to end of induction can also predict patients' outcome

- Longer follow-up is required before any final conclusion in particular regarding OS and the role of maintenance after ASCT

- Next analysis regarding FDG-PET will performed with the final analysis in 2016

LyMa project

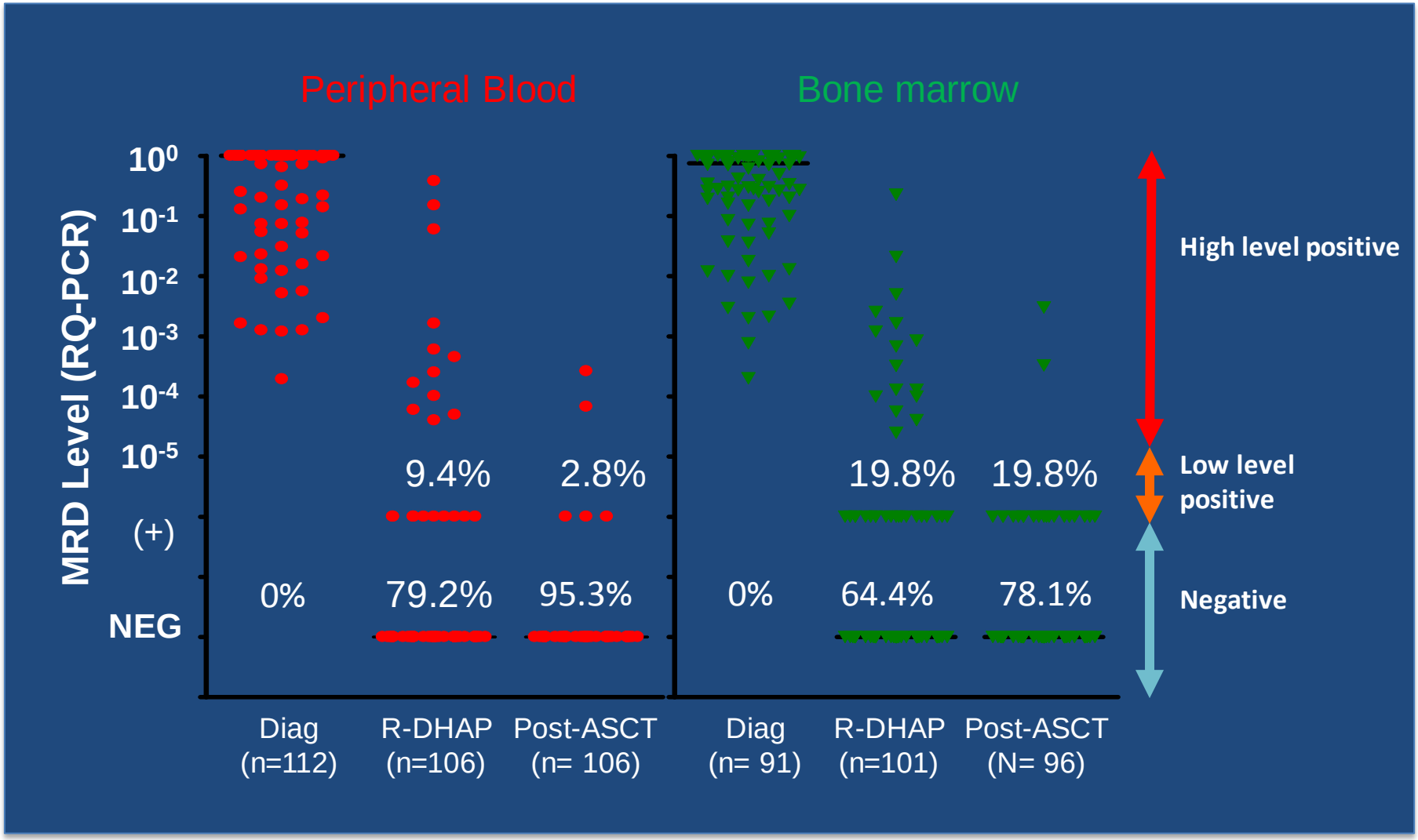
S. Le Gouill O. hermine	M. Callanan E Macintyre MH Delfau-Larue	C. Bodet-Milin M. Meignan	M. Maynadie	S. Minvielle	D. Canioni A. Moreau
LyMa Clinical trial	**LyMa MRD**	**LyMa FDG-TEP**	**LyMa Epidemiol.**	**LyMa Genomic**	**LyMa Envirron. Pathology**
Interim 2014 Final analysis 2016	Interim 2015 Final analysis 2017	Interim 2015 Final analysis 2017	Analysis 2016	Analysis 2016	Analysis 2017

Coordination: S. Le Gouill
Database LYSARC (S. Boussetta)
V. Rolland-Neyret (CP)

Lysa
THE LYMPHOMA STUDY ASSOCIATION

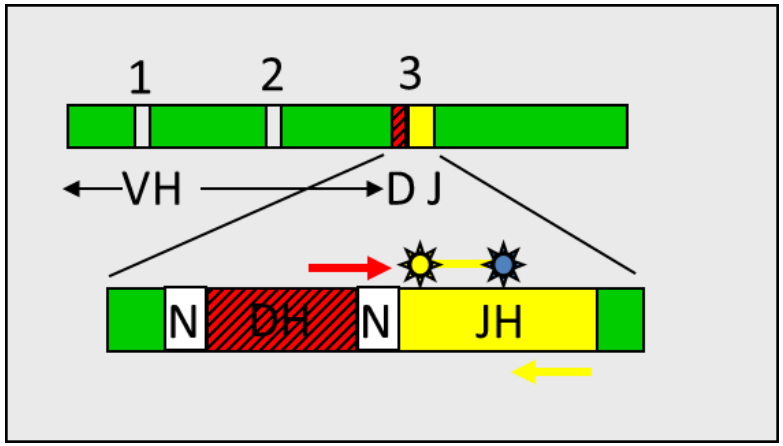
GOELAMS
Groupe Ouest-Est d'étude des Leucémies Aiguës et autres Maladies du Sang

PCR MRD



Callanan M. . …. Le Gouill s. ASH 2015, Orlando

- **MRD assay (ASO-*IGH* qPCR) :**



TGTGgatcgacGTATAGCAGCTTCGTCCTGGTTCGACCCCTGG

TGTGgatcgacGTATAGCAGCTTCGTCCTGGTTCGACCCCTGG

TGTGgatcgacGTATAGCAGCTTCGTCCTGGTTCGACCCCTGG

Quantitative range of 10-4 ; sensitive to 10-4 /10-5

EURO-MRD interpretation guidelines
French reference laboratories

MRD analysis in mantle cell lymphoma – state of the art in the clinic.

- Minimal residual disease (MRD) is emerging as a predictor of clinical outcome in patients with mantle cell lymphoma (MCL).
- Clinical utility in everyday clinical practice remains uncertain.
- MRD monitoring strategies and response criteria are not yet formally established.

-> LyMa-MRD project :
Prospective MRD monitoring in phase III trial in MCL (NCI NCT00921414)
(LYSA group).

(Nordic Group)

Pre-Emptive Treatment With Rituximab of Molecular Relapse After Autologous Stem Cell Transplantation in Mantle Cell Lymphoma

Niels S. Andersen, Lone B. Pedersen, Anna Laurell, Erkki Elonen, Arne Kolstad, Anne Marie Boesen, Lars M. Pedersen, Grete F. Lauritzsen, Roald Ekanger, Herman Nilsson-Ehle, Marie Nordström, Susanne Fredén, Mats Jerkeman, Mikael Eriksson, Jaan Vääri, Beatrice Mahler, and Christian H. Geisler

CLINICAL TRIALS AND OBSERVATIONS

(EU-MCL)

Molecular remission is an independent predictor of clinical outcome in patients with mantle cell lymphoma after combined immunochemotherapy: a European MCL intergroup study

Christiane Pott,[1] Eva Hoster,[2] Marie-Helene Delfau-Larue,[3] Kheira Beldjord,[4] Sebastian Böttcher,[1] Vahid Asnafi,[4] Anne Plonquet,[3] Reiner Siebert,[5] Evelyne Callet-Bauchu,[6] Niels Andersen,[7] Jacques J. M. van Dongen,[8] Wolfram Klapper,[9] Françoise Berger,[10] Vincent Ribrag,[11] Achiel L. van Hoof,[12] Marek Trneny,[13] Jan Walewski,[14] Peter Dreger,[15] Michael Unterhalt,[2] Wolfgang Hiddemann,[2] Michael Kneba,[1] Hanneke C. Kluin-Nelemans,[16] Olivier Hermine,[17] Elizabeth Macintyre,[4] and Martin Dreyling[2]

Non-Hodgkin's Lymphomas

(CALGB)

Articles and Brief Reports

Detection of minimal residual disease following induction immunochemotherapy predicts progression free survival in mantle cell lymphoma: final results of CALGB 59909

Hongtao Liu,[1] Jeffrey L. Johnson,[2] Greg Koval,[1] Greg Malnassy,[1] Dorie Sher,[1] Lloyd E. Damon,[3] Eric D. Hsi,[4] Donna Marie Bucci,[5] Charles A. Linker,[3] Bruce D. Cheson[6] and Wendy Stock[1]

[1]University of Chicago Medical Center; [2]Duke University Medical Center and CALGB Statistics and Data Center, Durham, NC; [3]University of California San Francisco; [4]Cleveland Clinic, Cleveland, OH; [5]The Ohio State University, Columbus, Ohio; and [6]Georgetown University Hospital, for the Cancer and Leukemia Group B (CALGB), Boston MA, USA

(LYSA-Goelams)

bjh research paper

Cloned *IGH VDJ* targets as tools for personalized minimal residual disease monitoring in mature lymphoid malignancies; a feasibility study in mantle cell lymphoma by the Groupe Ouest Est d'Etude des Leucémies et Autres Maladies du Sang.

Predictive power of early, sequential MRD monitoring in peripheral blood and bone marrow in patients with mantle cell lymphoma following autologous stem cell transplantation with or without Rituximab maintenance ; interim results from the LyMa-MRD project, conducted on behalf of the LYSA group.

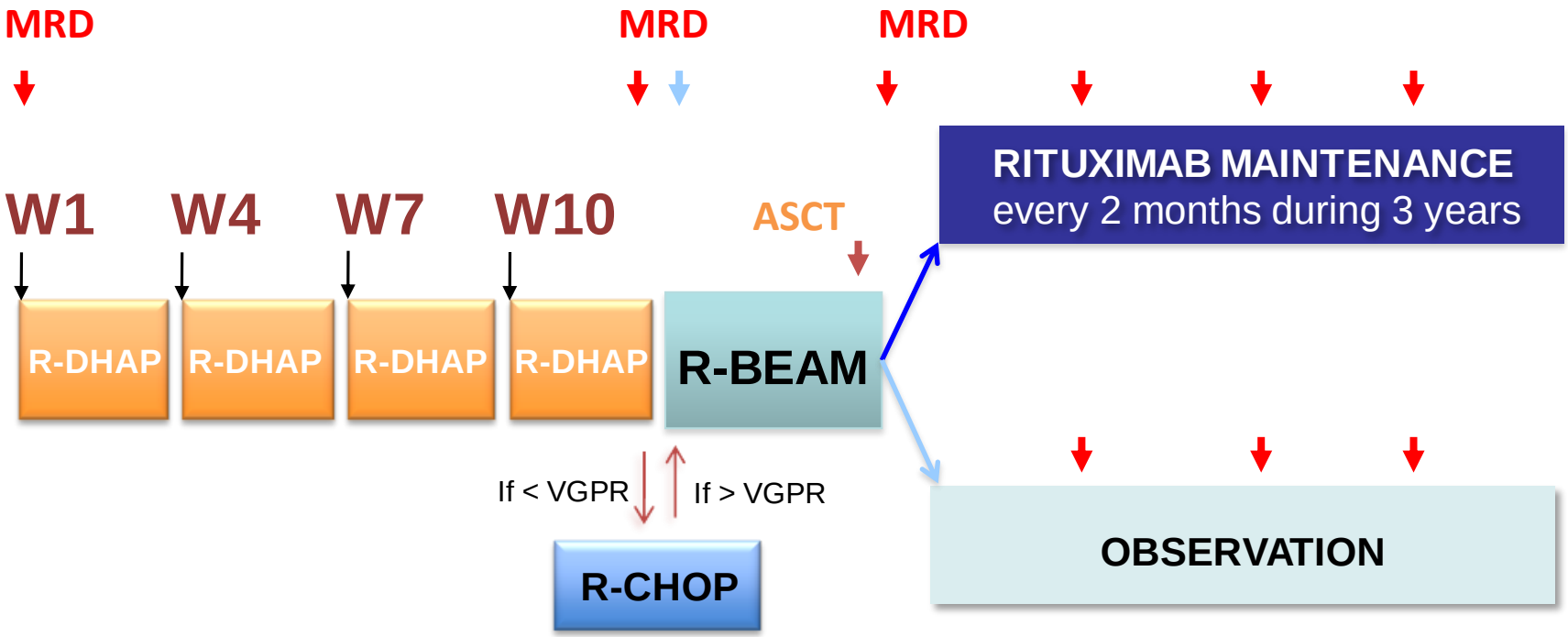
Mary Callanan, Marie-Hélène Delfau, Elizabeth Macintyre, Catherine Thieblemont, Lucie Oberic, Emmanuel Gyan, Krimo Bouabdallah, Rémy Gressin, Gandhi Damaj, Olivier Casasnovas, Vincent Ribrag, Estelle Gimenez, Olivier Hermine, Steven Le Gouill

(NCI NCT00921414; LyMa Trial).

Lysa
THE LYMPHOMA STUDY ASSOCIATION

Orlando, ASH 2015, Abstract 338

LyMa trial

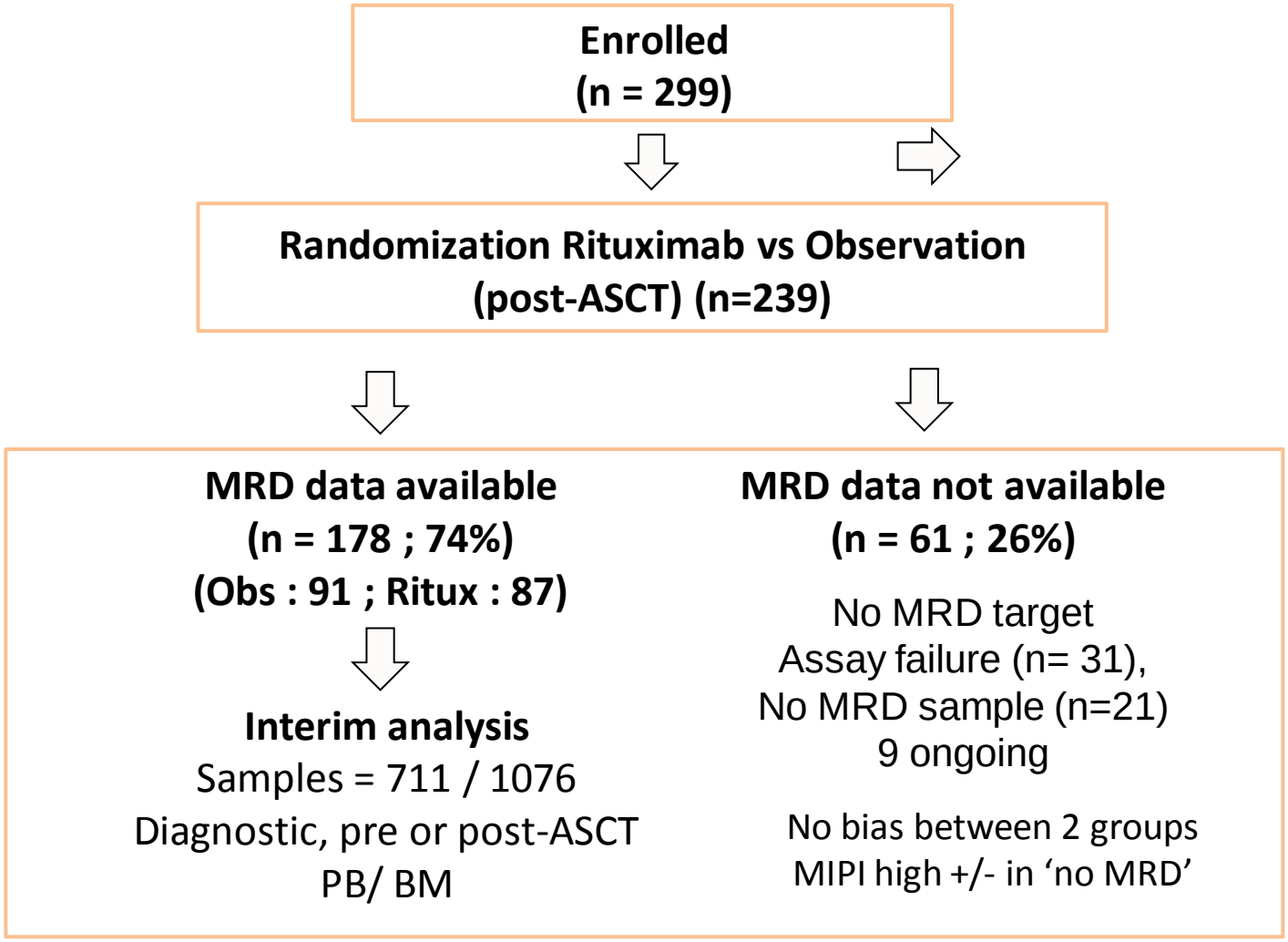


Interim analysis aim : prognostic impact of MRD status in peripheral blood (PB) and / or bone marrow (BM) pre- and post-ASCT on PFS

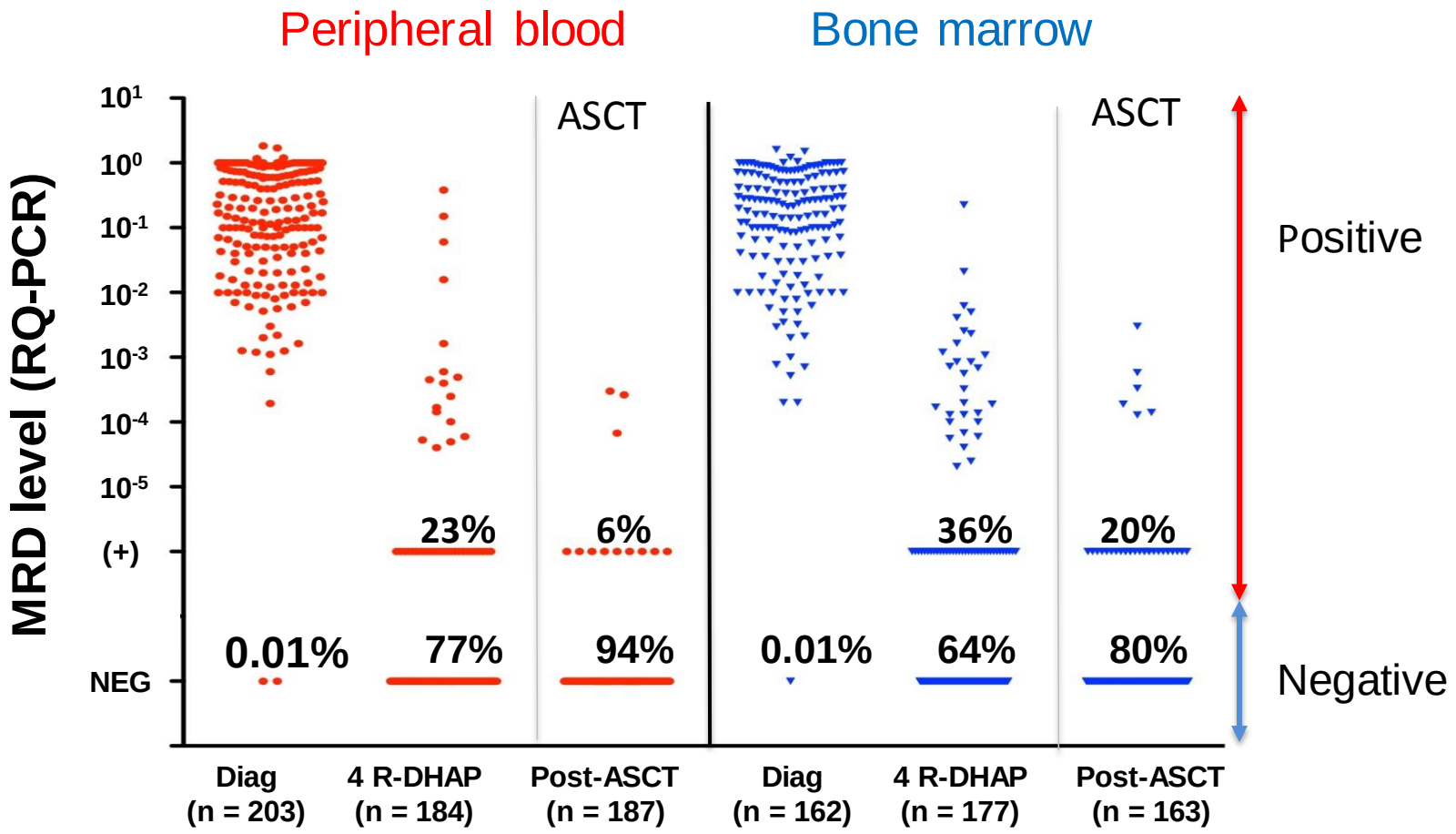
R-DHAP: Rituximab 375mg/m2; aracytine 2g/m2 x2 IV 3 hour injection 12 hour interval; dexamethasone 40mg d1-4; Cisplatin 100mg/m2 d1 (or oxaliplatin or carboplatin)

R-BEAM: Rituximab 500mg/m2 d-8; BCNU 300mg/m2 d-7; Etoposide 400mg/m2/d d-6 to -3; aracytine 400mg/m2/d d-6 to d-3; melphalan 140mg/m2 d-2

LyMa – MRD study cohort at interim analysis



MRD response rates pre / post-ASCT (LyMa Trial)

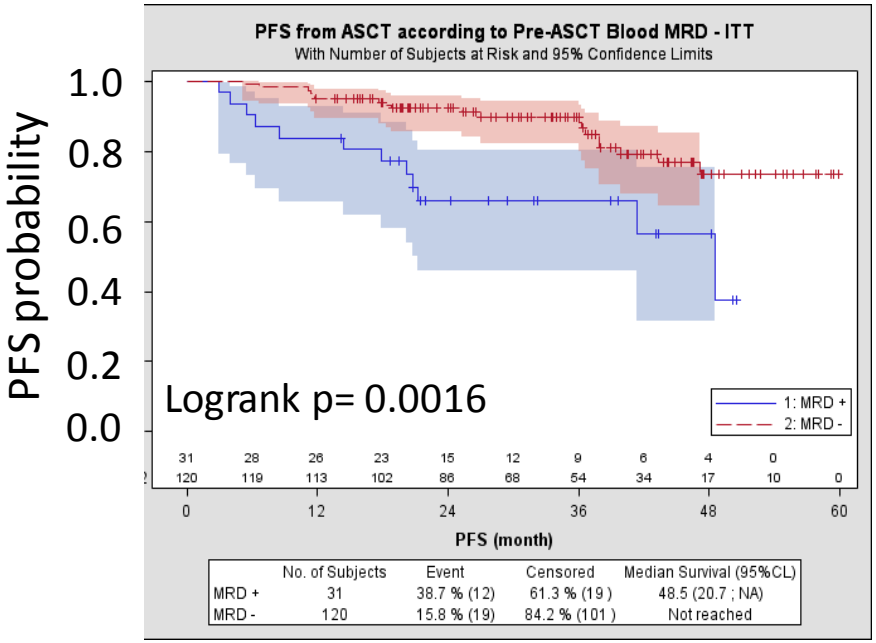


MRD current status (n= 217)
Samples at pre and post ASCT ; n = 1076)

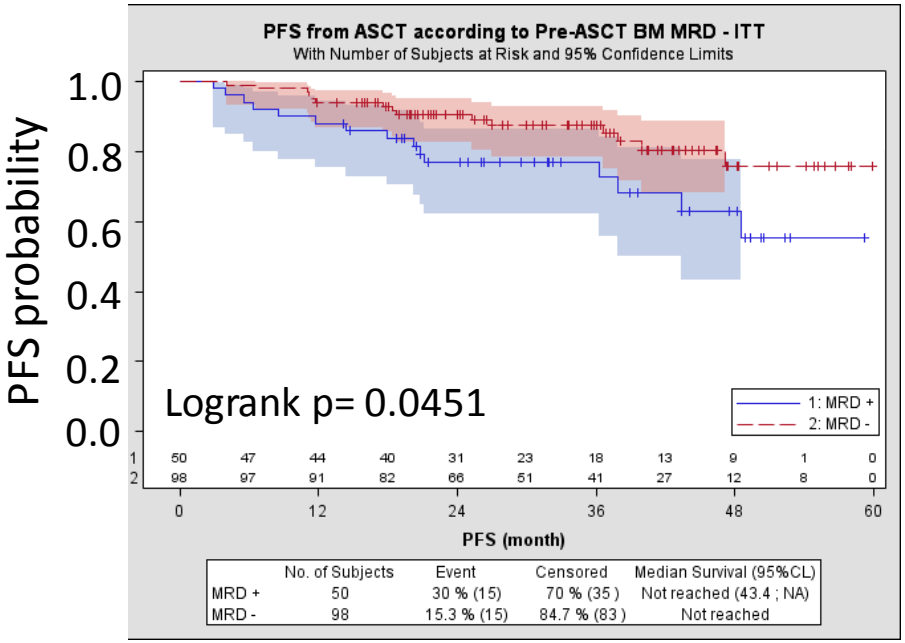
EURO-MRD : ASO *IGH* qPCR
Minimal assay sensitivity 10-4

PFS from ASCT according to pre-ASCT blood or bone marrow MRD - ITT

Blood

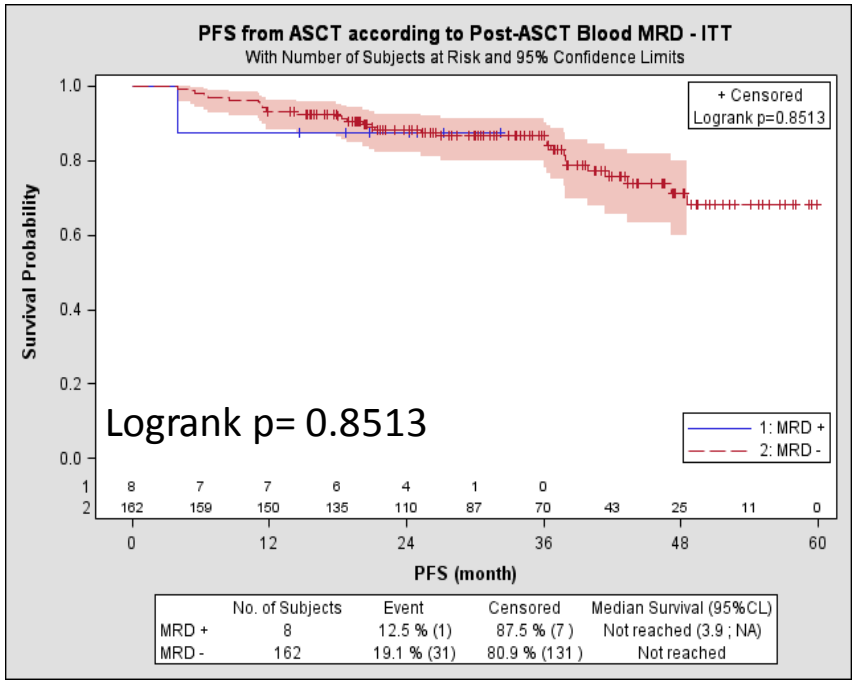


Bone marrow

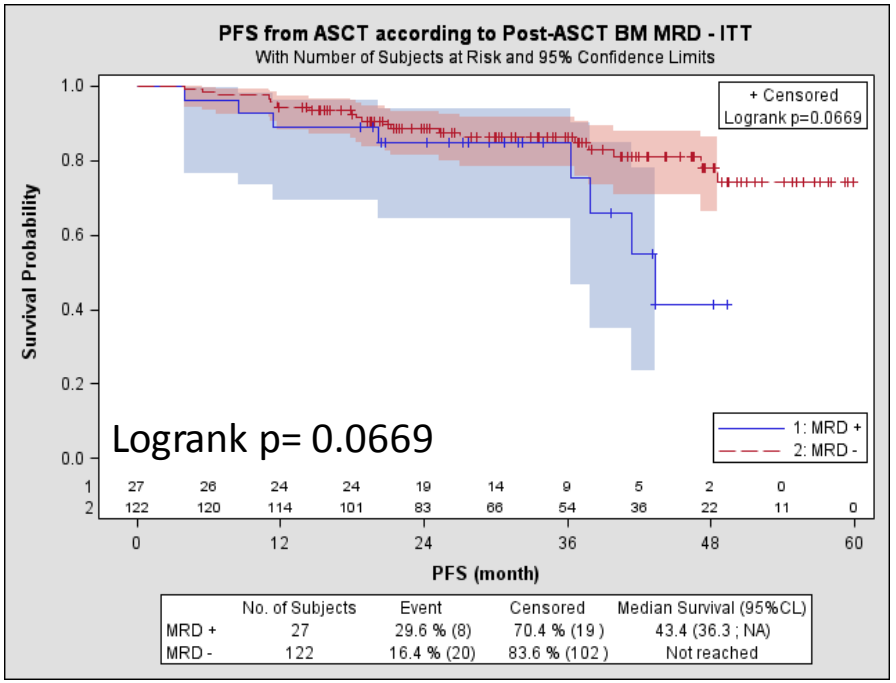


PFS according to post-ASCT blood or bone marrow MRD - ITT

Blood

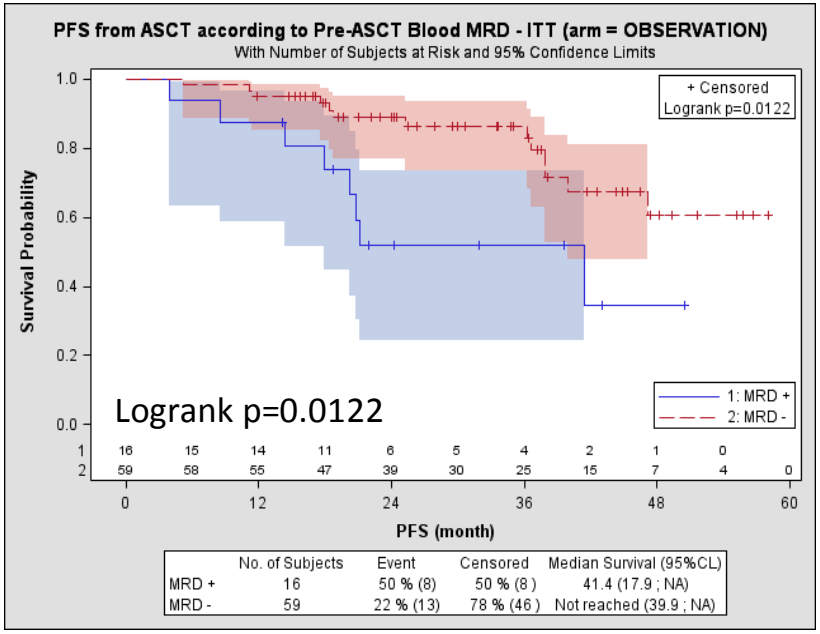


Bone marrow

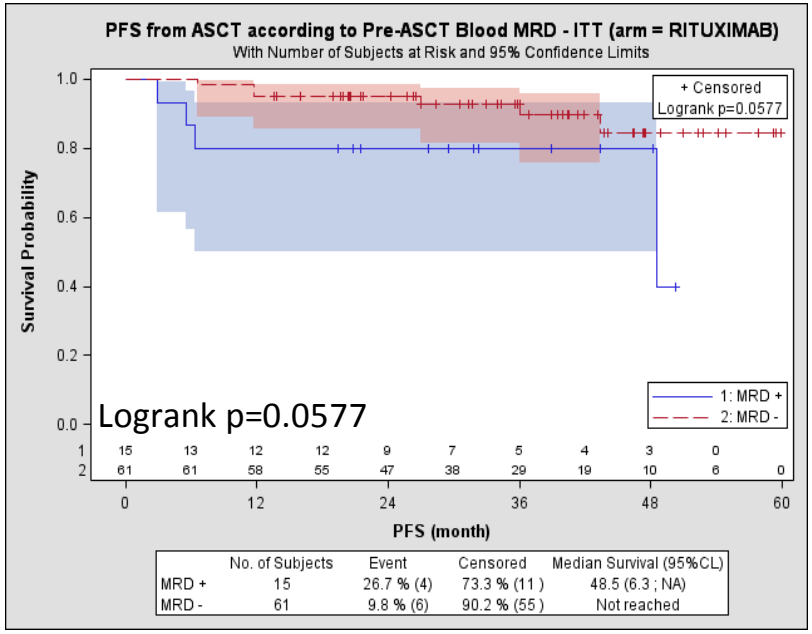


PFS from ASCT according to pre-ASCT blood MRD - ITT

Observation arm (n = 75)

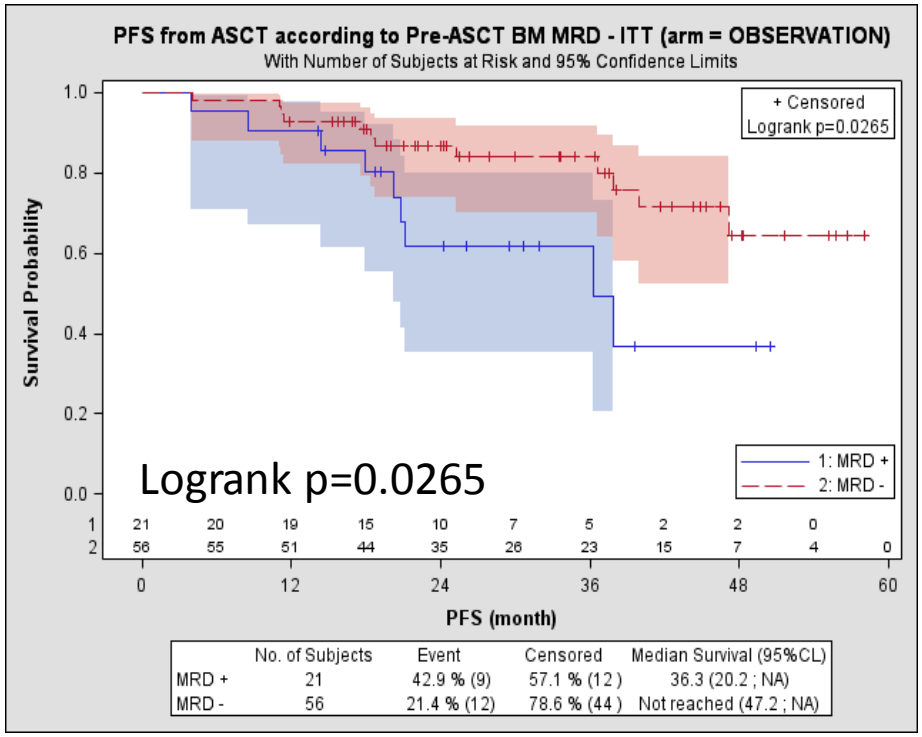


Rituximab maintenance arm (n = 76)



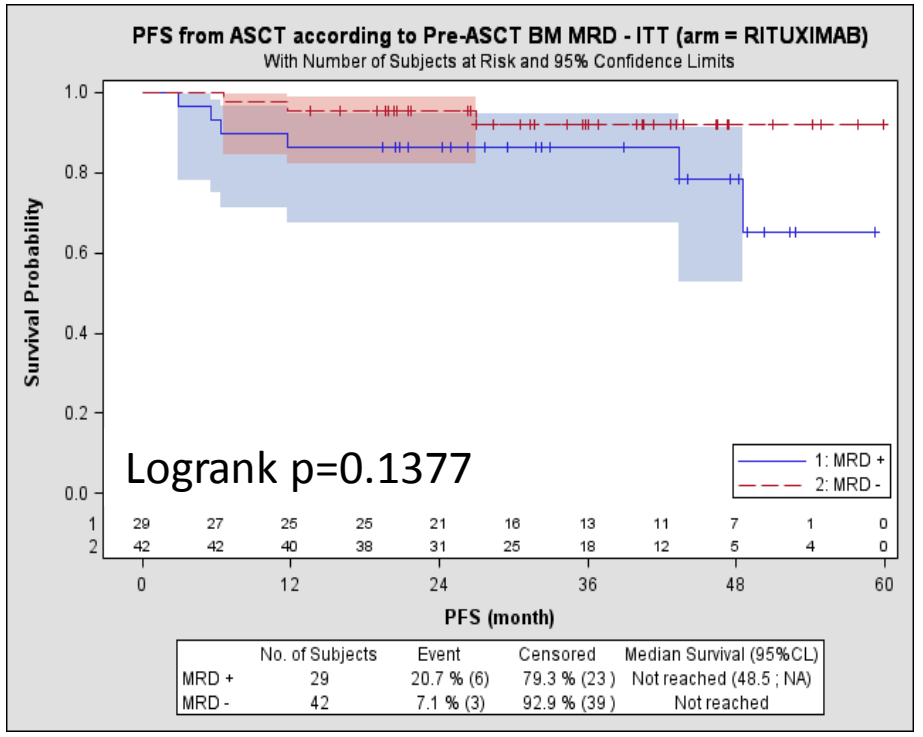
PFS from ASCT according to pre-ASCT bone marrow MRD - ITT

Observation arm (n = 77)



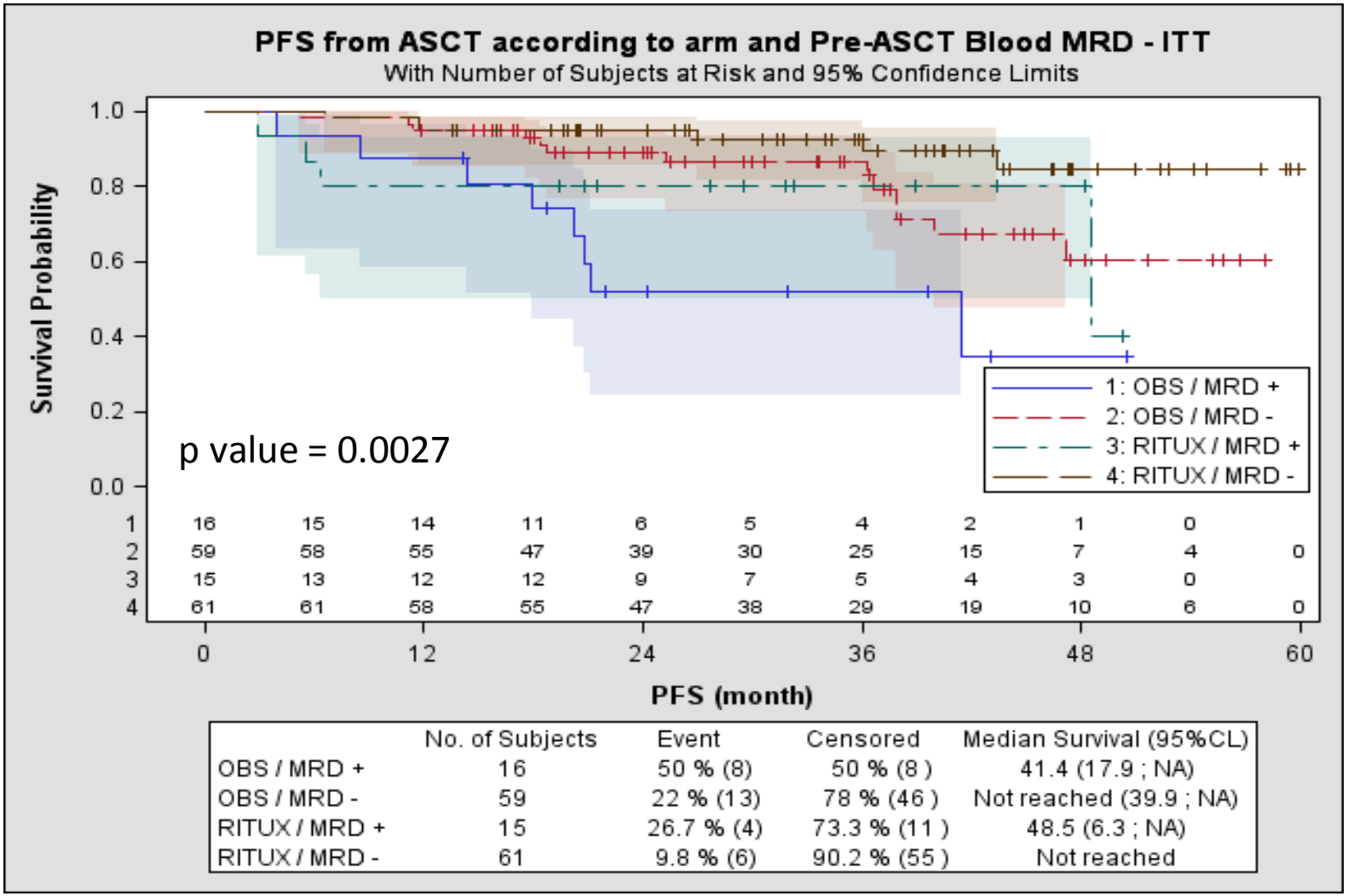
MRD neg = 73%

Rituximab maintenance arm (n = 71)



MRD neg = 59%

PFS from ASCT according to treatment arm and pre-ASCT blood MRD - ITT



	No. of Subjects	Event	Censored	Median Survival (95%CL)
OBS / MRD +	16	50 % (8)	50 % (8)	41.4 (17.9 ; NA)
OBS / MRD -	59	22 % (13)	78 % (46)	Not reached (39.9 ; NA)
RITUX / MRD +	15	26.7 % (4)	73.3 % (11)	48.5 (6.3 ; NA)
RITUX / MRD -	61	9.8 % (6)	90.2 % (55)	Not reached

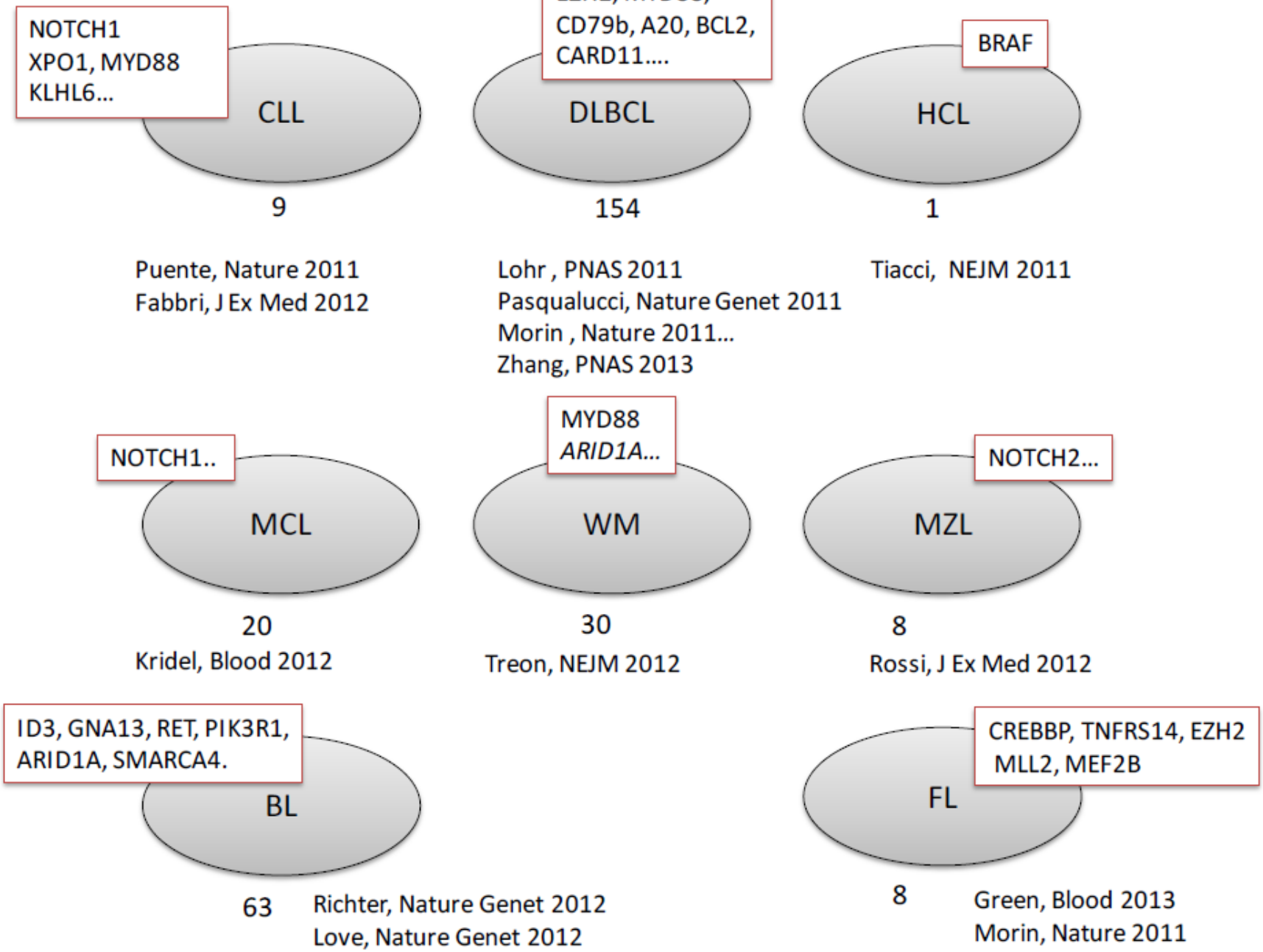
- Pre-ASCT MRD status in both BM and PB is an early predictor of PFS in younger MCL patients receiving ASCT.

- Early sequential MRD monitoring at the pre-ASCT treatment phase offers strong potential for early clinical outcome prediction and MRD-guided, risk-adapted treatment in future MCL trials.

- Rituximab maintenance provides longer PFS regardless of MRD status pre-ASCT suggestive of continued, clinically relevant anti-tumour activity of Rituximab against very rare residual circulating or ‘tissue-resident’ MCL cells.

Changer la stratégie thérapeutique par des nouveaux concepts et des nouvelles idées

NGS and NHL


NOTCH1
XPO1, MYD88
KLHL6…
CLL
9
Puente, Nature 2011
Fabbri, J Ex Med 2012
EZH2, MYD88,
CD79b, A20, BCL2,
CARD11….
DLBCL
154
Lohr , PNAS 2011
Pasqualucci, Nature Genet 2011
Morin , Nature 2011…
Zhang, PNAS 2013
BRAF
HCL
1
Tiacci, NEJM 2011
NOTCH1..
MCL
20
Kridel, Blood 2012
MYD88
ARID1A…
WM
30
Treon, NEJM 2012
NOTCH2…
MZL
8
Rossi, J Ex Med 2012
ID3, GNA13, RET, PIK3R1,
ARID1A, SMARCA4.
BL
63
Richter, Nature Genet 2012
Love, Nature Genet 2012
CREBBP, TNFRS14, EZH2
MLL2, MEF2B
FL
8
Green, Blood 2013
Morin, Nature 2011

MIPI : age, LDH, Ann Arbor, lymphocytosis or bio-MIPI (Ki67)

Genomic ?

Epigenomic ?

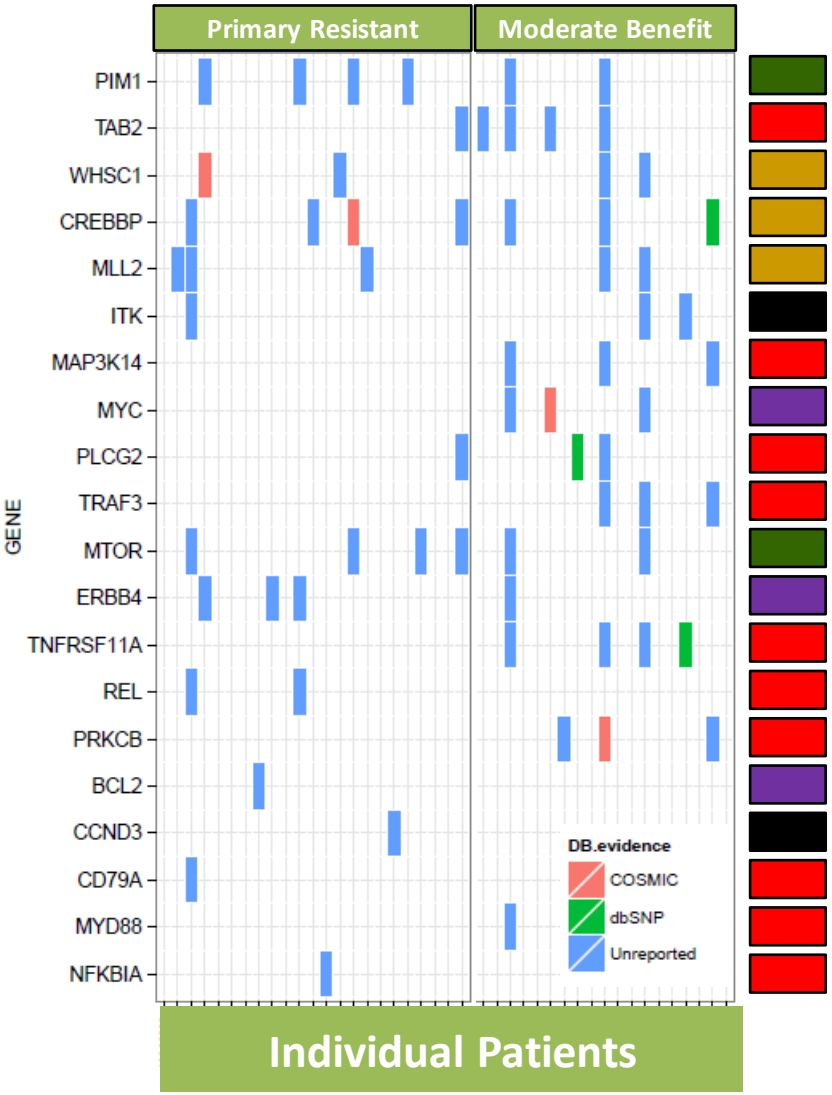
Proteomic ?

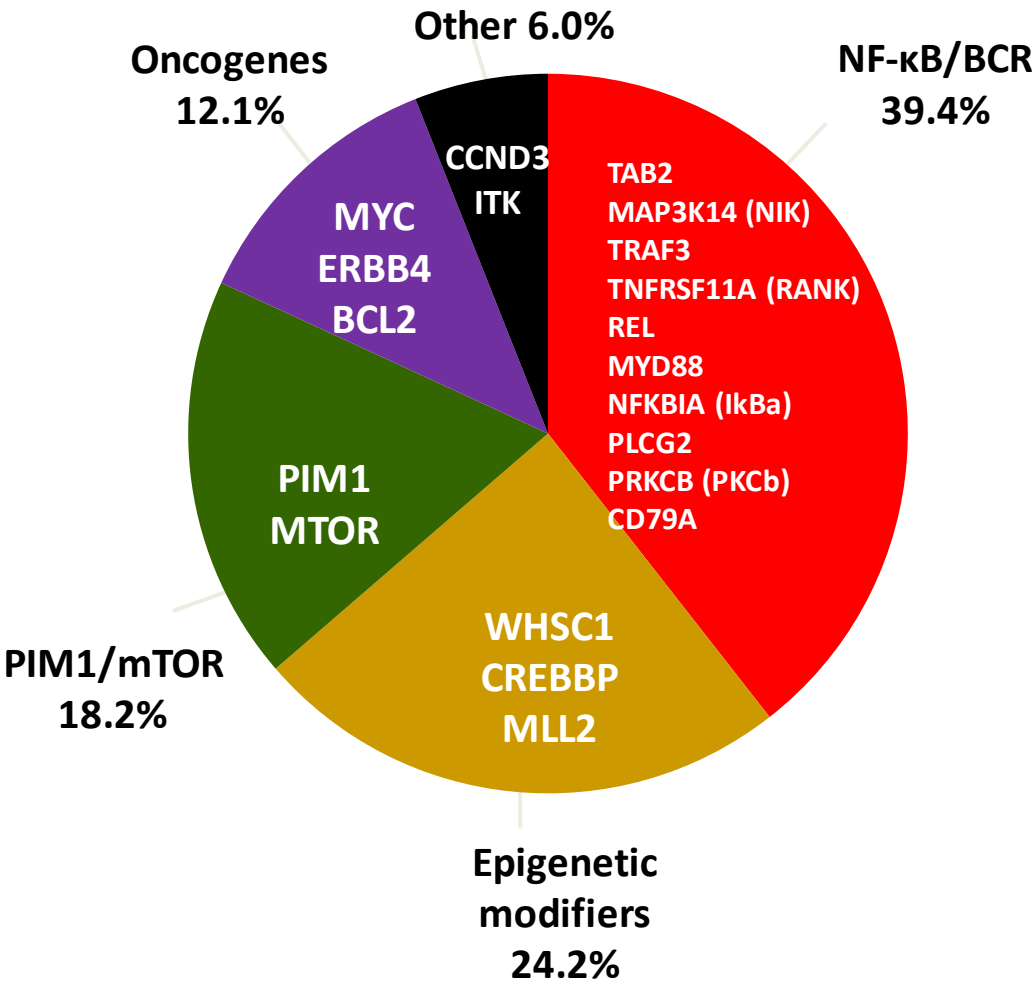
Biologic dysregulated system

≠

NF-κB, PIM / mTOR, and Epigenetic Modifiers

Differential mutations

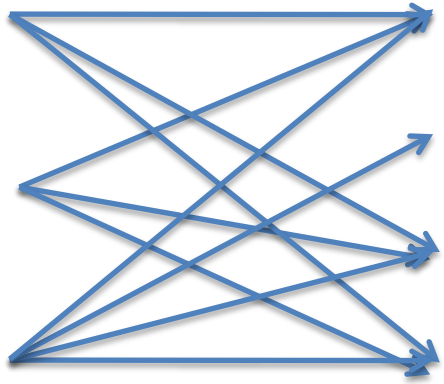




Balasubramanian et al., ASH 2014; abstract 78 (oral presentation)

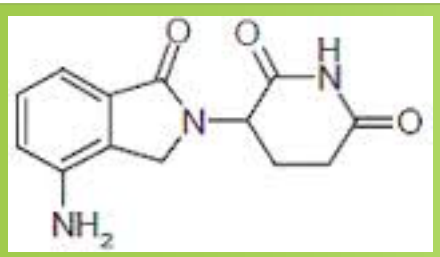
R-chemo + Chemo-free options + Rituximab

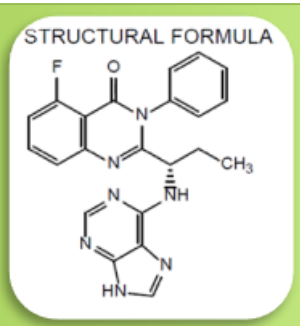
- Aracytine
- Bendamustine
- Anthracycline

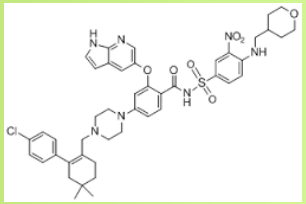


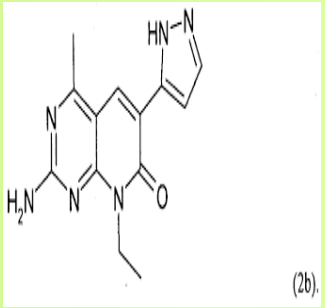
- Velcade:
- Lenalidomide
- Torisel
- Ibrutinib

MORE ACTIVE DRUGS

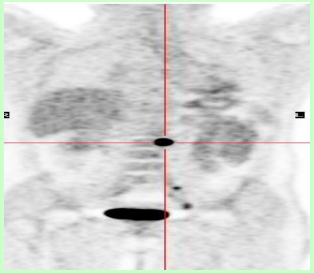


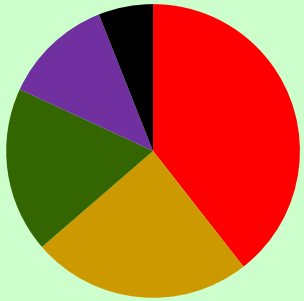


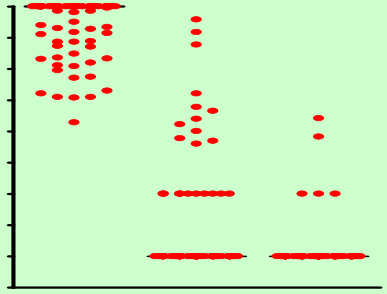




MORE PREDICTIVE TOOLS







…. BUT LESS MONEY !!!!

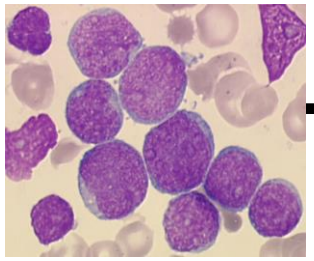
One line of treatment should not jeopardize treatment options at relapse

« As military strategists go Duke, you are not exactly Alexander the Great »

Risk-adapted targeted strategy over time

1

High Risk of relapse MCL patients ?



2

Response at mid-term ?

3

Response at end of therapy ?

4

MRD monitoring

Chemo /Chemo free

GO

NO GO

GO

NO GO

1

New biomarkers:
NGS
MIPI
PET
Ki67
siRNA
Genetic abnormalities ...

2

New salvage treatments:
Temsirolimus
Velcade
Revlimid
BTK-inhibitors ...

3

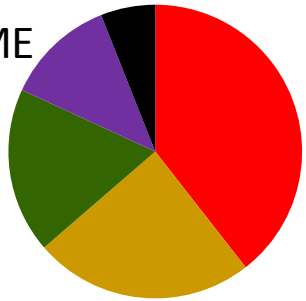
New salvage Treatments:
Temsirolimus
Velcade
Revlimid
BTK-inhibitors ...

4

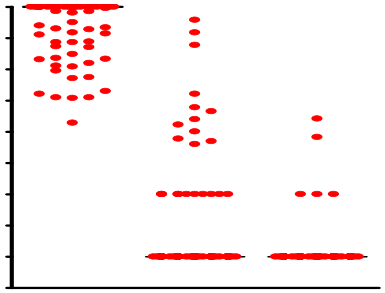
pre-emptive treatment of clinical relapse:
Rituximab
Velcade
Temsirolimus
BTK ...

COHORTES DE PATIENTS

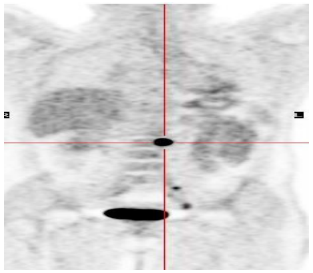
WHOLE GENOME/EPIGENOME /bio-mol



MRD monitoring



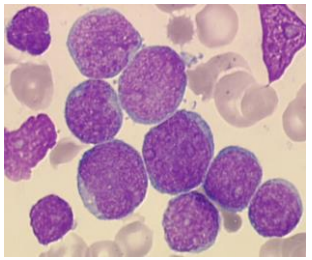
IMAGERIE



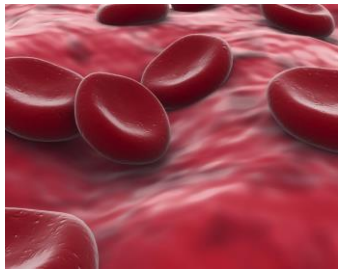
DATA-CENTER

Lysa
THE LYMPHOMA STUDY ASSOCIATION

Données cellulaire et environnement



Epidemio et société



Marqueurs sanguins (ARN, ADN tumoral)

DATA-CENTER

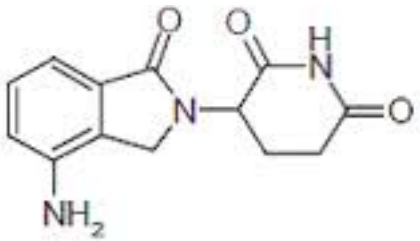
Lysa
THE LYMPHOMA STUDY ASSOCIATION

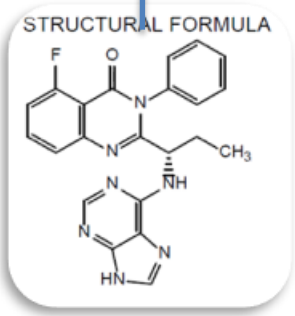
Analyse big data

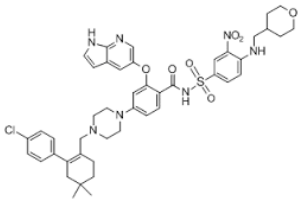
Détermination des profils « LCM »

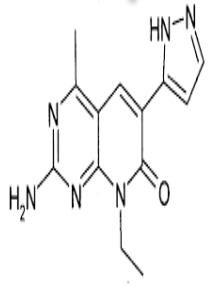
biologie des systèmes

Modélisation cellulaire in vitro et bio-informatique du LCM







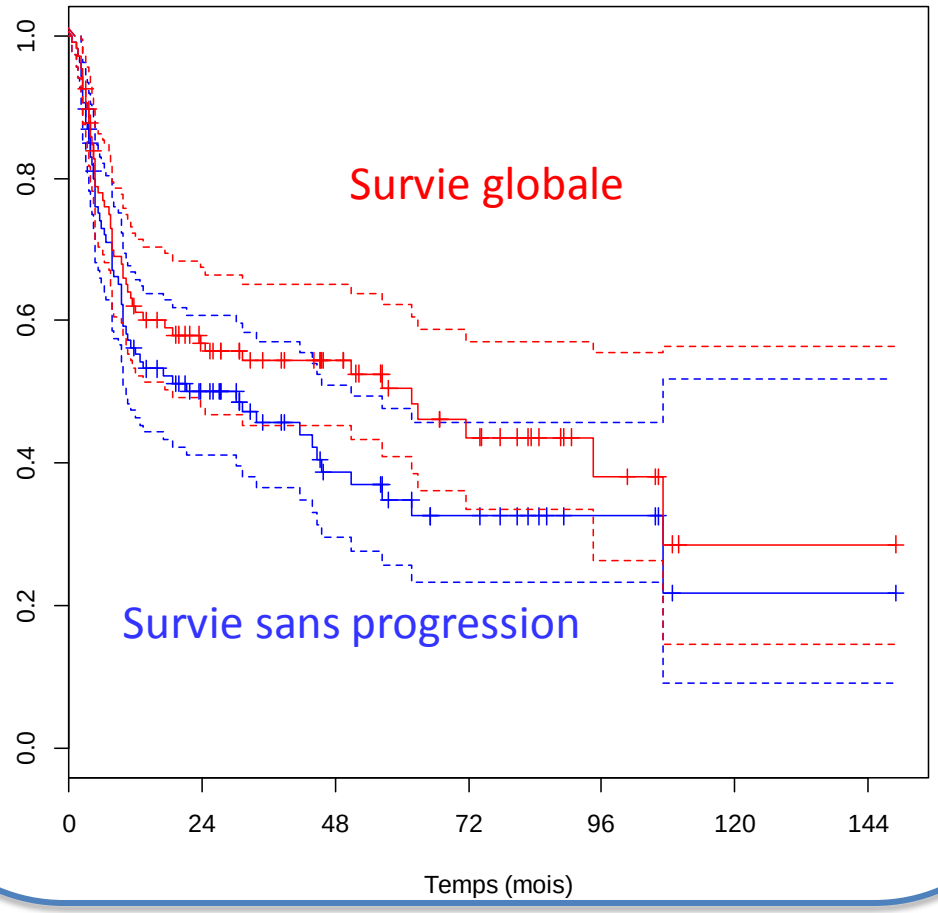


(2b).


Lysa
THE LYMPHOMA
STUDY ASSOCIATION

Résultats

Suivi médian: 45m



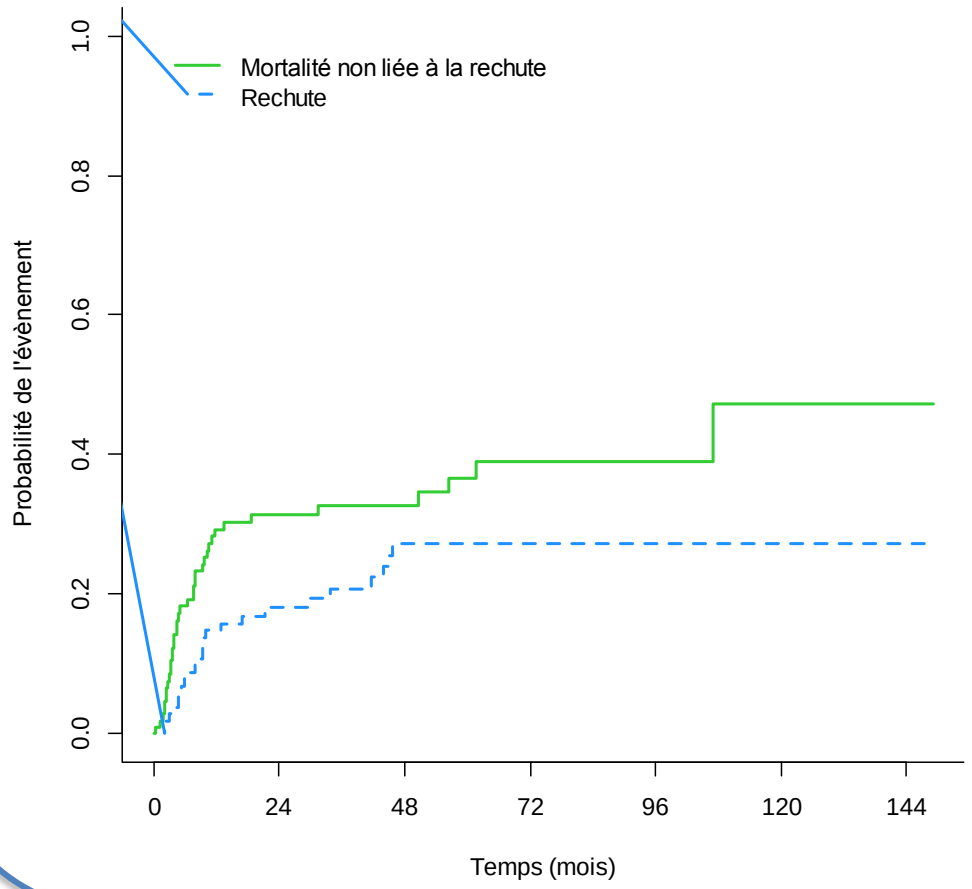
SG médiane: 62m

SG à 5 ans: 51%

SSP médiane: 30,1m

SSP à 5 ans: 35%

Mortalité toxique et rechute



6m: 18%

3 ans: 33%

aGVH Grade III/IV: 20 (19%)

cGVH Ext. : 28 (29%*)

Rechute: 24 (24%)

Mortalité toxique et rechute