Azienda Ospedaliera Nazionale
SS. Antonio e Biagio e Cesare Arrigo
Alessandria

Firenze, 16th September 2016

Marco Ladetto MD, Az Osp Santi Antonio e Biagio e Cesare Arrigo, Alessandria, Italy EU

Novita da EHA 2016 – Copenhagen

Linfomi

THREE QUESTIONS TO ADDRESS:

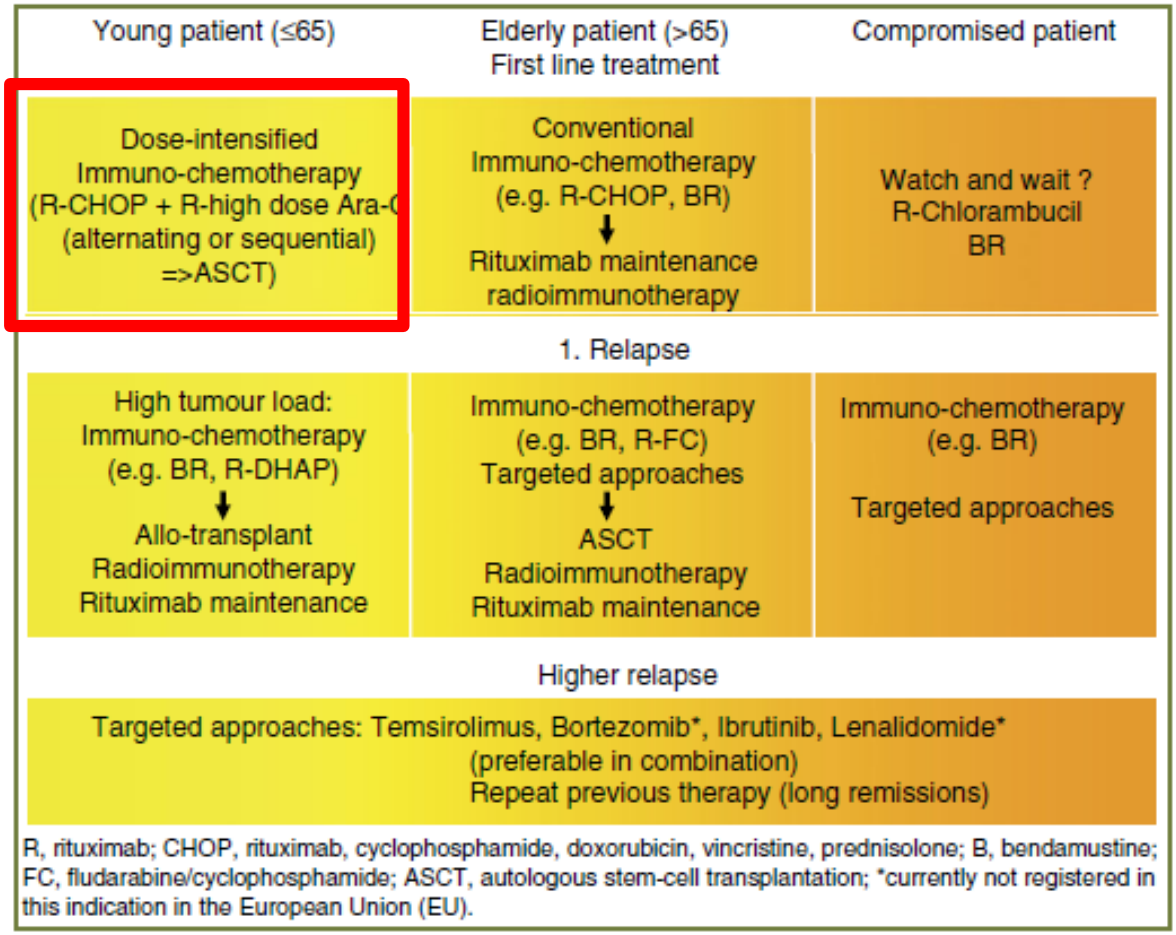
1. **Is ASCT still the golden standard for MCL? And how to challenge it in the future?**
2. **What is new in relapsed follicular lymphoma? Is benda-obinotuzumab a major step forward? Which are the alternatives?**
3. **Ultra high-risk lymphoma patients: Can we identify them? And where shall we go for treatment?**

THREE QUESTIONS TO ADDRESS:

1. **Is ASCT still the golden standard for MCL? And how to challenge it in the future?**
2. **What is new in relapsed follicular lymphoma? Is benda-obinotuzumab a major step forward? Which are the alternatives?**
3. **Ultra high-risk lymphoma patients: Can we identify them? And where shall we go for treatment?**

Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

M. Dreyling[1], C. Geisler[2], O. Hermine[3], H. C. Kluin-Nelemans[4], S. Le Gouill[5], S. Rule[6], O. Shpilberg[7], J. Walewski[8] & M. Ladetto[9], on behalf of the ESMO Guidelines Working Group*



R, rituximab; CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone; B, bendamustine; FC, fludarabine/cyclophosphamide; ASCT, autologous stem-cell transplantation; *currently not registered in this indication in the European Union (EU).

MCL Educational session

Points raised by prof E Zucca in the educational session EHA2016

Copenhagen

1. **Watch and wait?**
2. **Prognosticators and prognostic models**
3. **Role of MRD**
4. **Role of PET**

MCL Educational session

Conclusions from prof T. Robak in the educational session EHA2016

Copenhagen

1. **Heterogeneity and personalization**
2. **OS is improving**
3. **Target drugs are effective in the R/R setting**
4. **Auto ASCT and allo-SCT should be considered also at relapse**

Leaders in Hematology review series

The role of targeted treatment in mantle cell lymphoma: is transplant dead or alive?

Martin Dreyling[1] and Simone Ferrero,[2] on behalf of European Mantle Cell Lymphoma Network

[1]Department of Medicine III, Hospital of the University LMU München, Germany; and [2]Division of Hematology, Department of Molecular Biotechnologies and Health Sciences, University of Torino, Italy

Haematologica, 2016

YOUNG PATIENTS PROBABLY NOT DESERVING ASCT

- ✓ **Patients with major comorbidities**
- ✓ **Patients with limited stage MCL**
- ✓ **Indolent MCL**
- ✓ **Primary refractory patients**

For specific prognostic subgroups….

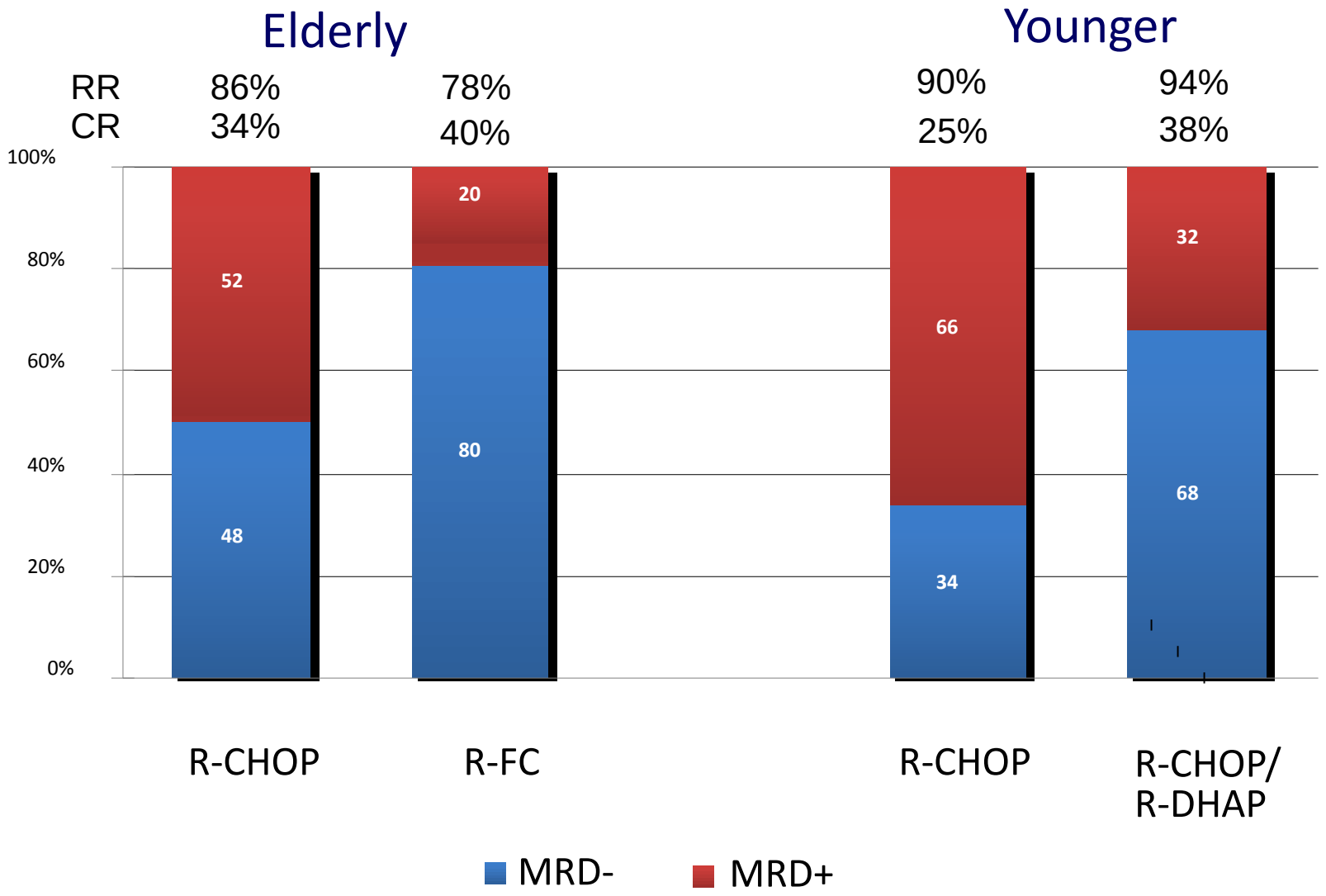
NOT YET

Table 1. Published clinical studies investigating first-line dose-intensified therapy in MCL.

	Author	Study Features	Evaluable patients	Therapeutic regimen	ORR% (CR%)	Median PFS (years)	Median OS (years)	Dropout rate	TRM	Secondary tumors rate
ASCT Based regimens	Dreyling *et al.*, 2005 [18]	Phase III, randomized	122	R-CHOP + TBI + ASCT *vs.* R-CHOP + TBI + interferon-α	98 (81) *vs.* 99 (37)	3,3 *vs.* 1,4	NR (83% 3-y OS) *vs.* NR (77% 3-y OS)	13% *vs.* na	5% *vs.* 0%	5%
	Hermine *et al.*, 2012 [34]	Phase III, randomized	455	R-CHOP + TBI + ASCT *vs.* R-CHOP/R-DHAP + HD-araC + ASCT	98 (63) *vs.* 99 (61)	3,8 *vs.* 7,3	6,8 *vs.* NR	na	4%	na
	Damon *et al.*, 2009 [26]	Phase II	77	R-CHOP + methotrexate + HD-araC/etoposide + ASCT	88 (69)	NR (56% 5-y PFS)	NR (64% 5-y OS)	13%	3%	na
	Van't Veer *et al.*, 2009 [27]	Phase II	87	R-CHOP + HD-araC + ASCT	70 (64)	NR (36% 4-y PFS)	NR (66% 4-y OS)	30%	5%	na
	Geisler *et al.*, 2012 [39]	Phase II	160	R-Maxi-CHOP + HD-araC+ ASCT	96 (54)	7,4	NR (64% 10-y OS)	9%	5%	4%
	Delarue *et al.*, 2013 [28]	Phase II	60	R-CHOP/R-DHAP + HD-araC + ASCT	100 (96)	6,9	NR (75% 5-y OS)	18%	1,5%	18%
	Touzeau *et al.*, 2013 [29]	Retrospective	396	Different ASCT-based schedules	83 (77)	NR (67% 3-y PFS)	NR (83% 3-y OS)	na	2,5%	6%
	Kolstad *et al.*, 2014 [40]	Phase II	160	R-Maxi-CHOP + HD-araC+/- Zevalin + ASCT	94 (82)	R (71% 4-y PFS)	NR (78% 4-y OS)	9%	6%	3%
	Le Gouill *et al.*, 2014 [42]	Phase III, randomized	299	R-DHAP + ASCT +/- rituximab maintenance	na (92)	R (74% 3-y PFS)	NR (83% 3-y OS)	14%	na	na
	Cortelazzo *et al.*, 2015* [99]	Phase III, randomized	260*	R-CHOP+R-CTX+HD-araC+ASCT +/- lenalidomide maintenance	86 (78)	R (78% 2-y PFS)	NR (89% 2-y OS)	22%*	2%	na
Non-ASCT based regimens	Romaguera *et al.*, 2010 [6]	Phase II, monocentric	97	R-Hyper-CVAD	97 (87)	4,6	NR (64% 10-y OS)	29%	8%	5%
	Merli *et al.*, 2012 [31]	Phase II, multicentric	60	R-Hyper-CVAD	83 (72)	R (73% 5-y PFS)	NR (61% 5-y OS)	63%	6,5%	1,5%
	Bernstein *et al.*, 2013 [32]	Phase II, multicentric	49	R-Hyper-CVAD	86 (55)	4,8	6,8	39%	2%	4%

Adapted from Dreyling M and Ferrero S, 2016

MRD response after induction



Courtesy of Christiane Pott

Eskeund CW S437
15-YEAR FOLLOW-UP OF THE NORDIC MCL2-TRIAL: DESPITE LONG-TERM RESPONSES LATE RELAPSES STILL OCCUR

BACKGROUND

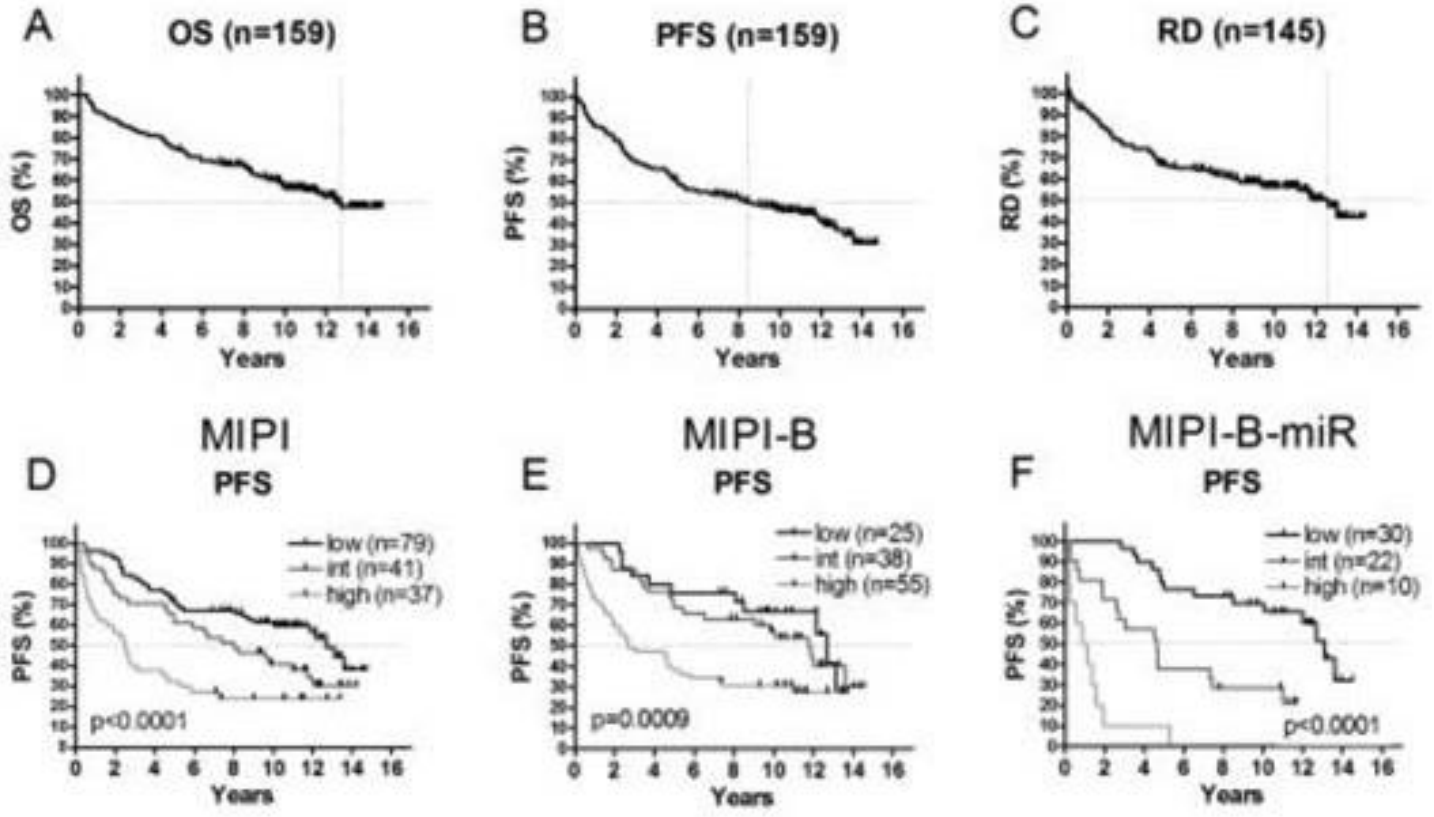
- Outcome of MCL has has improved thanks to Ara-C and R
- the Nordic trial showed a projected 10-year OS and PFS of 58% and 43%
- **Updated results at a median follow-up of 11.4 years**

METHODS

- 160 untreated stage II-IV MCL pts.
- maxi-CHOP alternated to high-dose Ara-C, BEAM/BEAC and ASCT in responders (n=145).
- Use of pre-emptive rituximab (Andersen, JCO, 2009)

RESULTS

- **the median OS and PFS were 12.7 and 8.5 years**.
- RD of the 145 patients who underwent ASCT was 12.4 years
- micro-RNA-18b (MIPI-B-miR) remains highly significant and identifies a high-risk group of an exceedingly poor prognosis with OS and PFS of only 1.6 and 1.0 years



CONCLUSIONS

- **a pattern of continuing relapse is observed, seemingly precluding cure**.

- MIPI, MIPI-B and, in particular, MIPI-B-miR remain valid prognosticators that clearly separate patients into risk groups with different outcomes.

- All risk groups might benefit from addition of novel agents.

Rule S et al S438
OS OUTCOMES IN PTS WITH MCL TREATED WITH IBRUTINIB IN A POOLED ANALYSIS OF 370 PATIENTS FROM 3 INTERNATIONAL OPEN-LABEL STUDIES

BACKGROUND

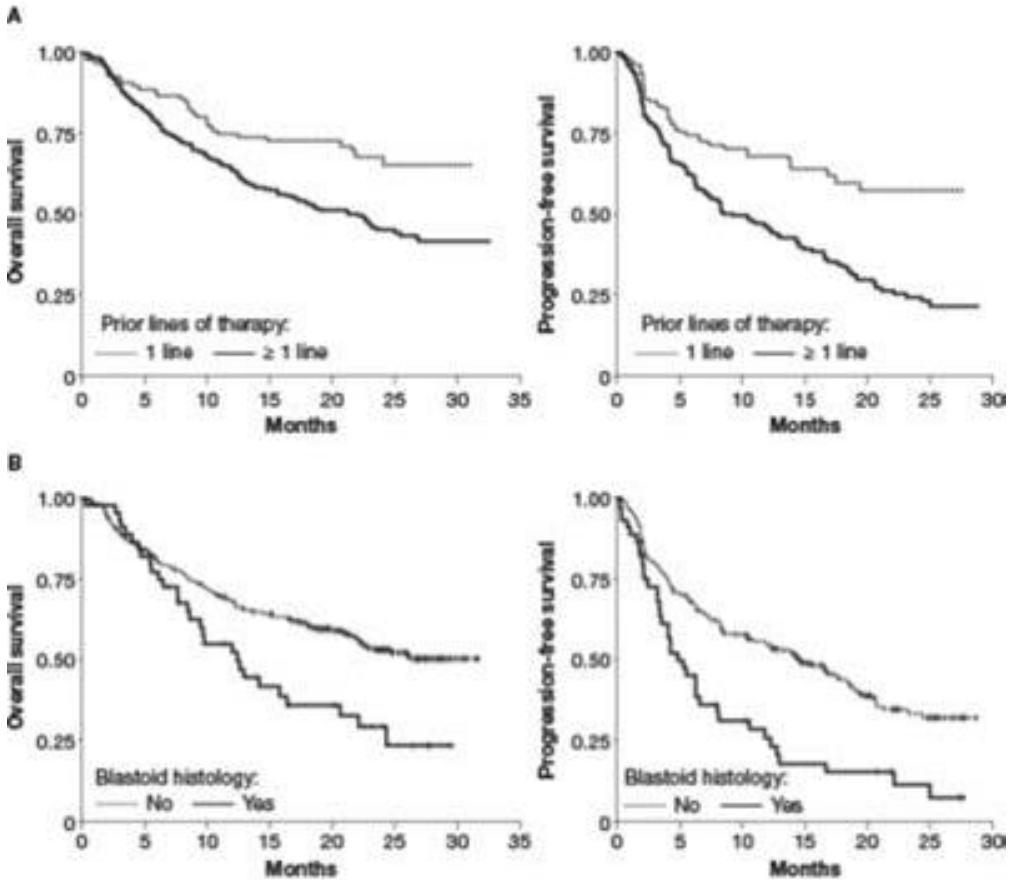
•pooled analysis from 3 ibrutinib studies (PCYC-1104, MCL2001 [SPARK] and MCL3001 [RAY])

METHODS

- ibrutinib 560 mg orally
- Inclusion and exclusion criteria were similar
- Simple descriptive statistics and exploratory analyses were done for PFS and OS with univariate and multivariate analyses

RESULTS

- 370 patients were included in this analysis; median age was 67.5 years, 94%.
- 27%, 29%, 22% had 1, 2, 3 prior lines of therapy.
- Overall response rate (ORR) was 66% (20% CR; 46% PR),
- ORR for patients with 1, 2 and ≥3 prior lines of therapy was 77% , 71% and 64%
- DOR, PFS and OS of 18.6, 12.8 and 25.0 months,
- CR pts, had a PFS of 70% and OS of 90% at 2 years.
- ECOG, sMIPI, bulky disease and blastoid histology impacts OS



CONCLUSIONS

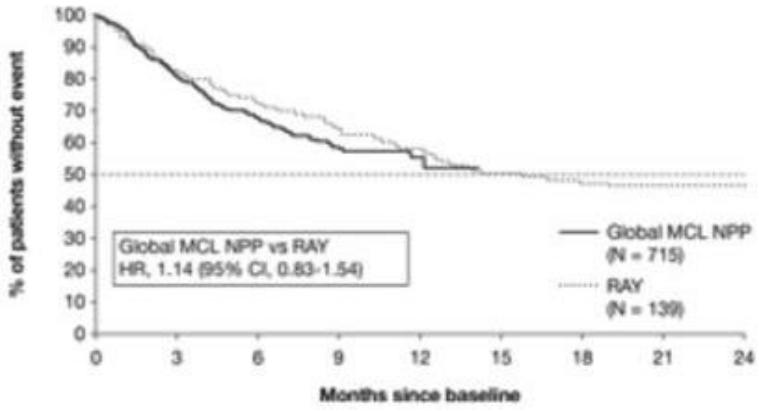
OS is better patients who are younger and who have fewer prior lines of therapy

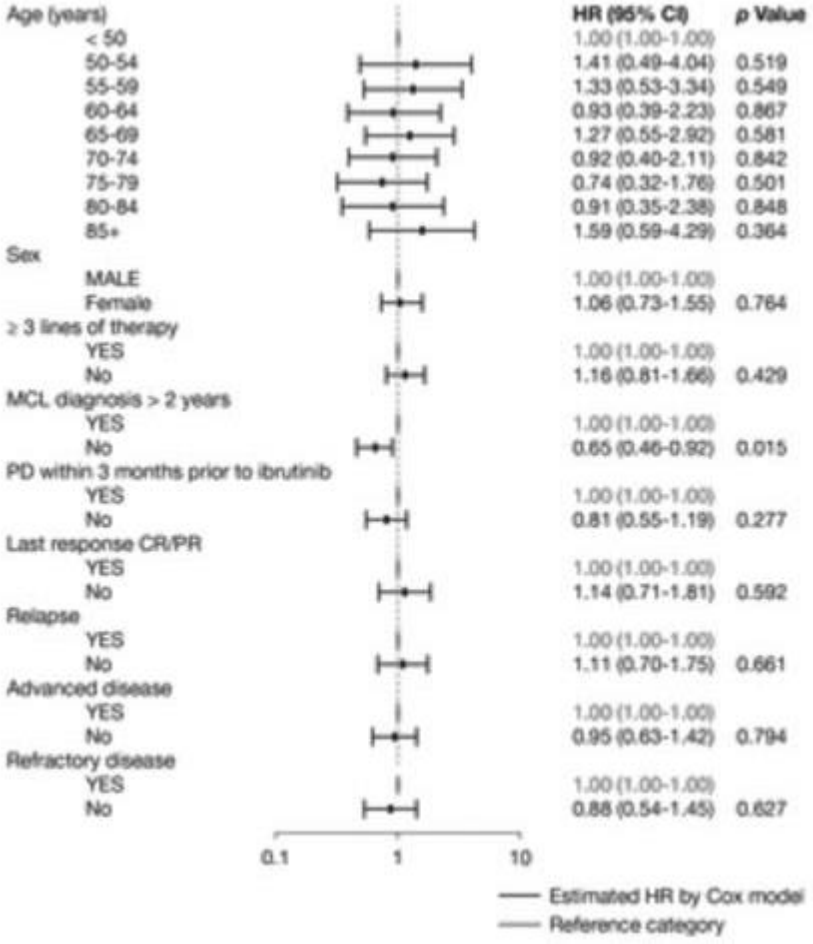
Ibrutinib is an effective agent in blastoid MCL to achieve a response and potentially provide a bridge transplant.

Data support the preferential use of ibrutinib after initial vs later relapse

Rule S et al P699
REAL-WORLD EXPERIENCE OF IBRUTINIB IN >700 PATIENTS WITH MANTLE-CELL LYMPHOMA: DATA FROM A GLOBAL NAMED PATIENT PROGRAM

•NPP program to allow access to ibrutinib for eligible patients R/E MCL This program provides real-world data on estimated outcomes with ibrutinib across a large, global MCL population.





Lenz G et al S439
SEQUENCE VARIANTS IN PATIENTS WITH PRIMARY AND ACQUIRED RESISTANCE TO IBRUTINIB IN THE PHASE 3 MCL3001 (RAY) TRIAL

BACKGROUND

•To identify specific mechanisms of ibrutinib resistance in MCL, and to correlate genetic signatures with patient response.

METHODS

- Primary resistance analysis,
- Acquired resistance analysis.

RESULTS

Mutations associated with primary resistance to ibrutinib were identified in NF-kB signaling pathways, both canonical (e.g., A20) and non-canonical (e.g., BIRC2). Other mutations were found in epigenetic modifiers and in the EGFR family.

Acquired resistence: Mutations in epigenetic modifiers and alternate NF-kB or PI3K/mTOR pathways were found after a short treatment duration (<4 months).

No primary or secondary BTK C481S mutations

CONCLUSIONS

Understanding both primary and acquired resistance patterns is key in order to improve outcomes and define the populations that benefit from ibrutinib treatment

THREE QUESTIONS TO ADDRESS:

1. **Is ASCT still the golden standard for MCL? And how to challenge it in the future?**
2. **What is new in relapsed follicular lymphoma? Is benda-obinotuzumab a major step forward? Which are the alternatives?**
3. **Ultra high-risk lymphoma patients: Can we identify them? And where shall we go for treatment?**

THE GADOLIN TRIAL

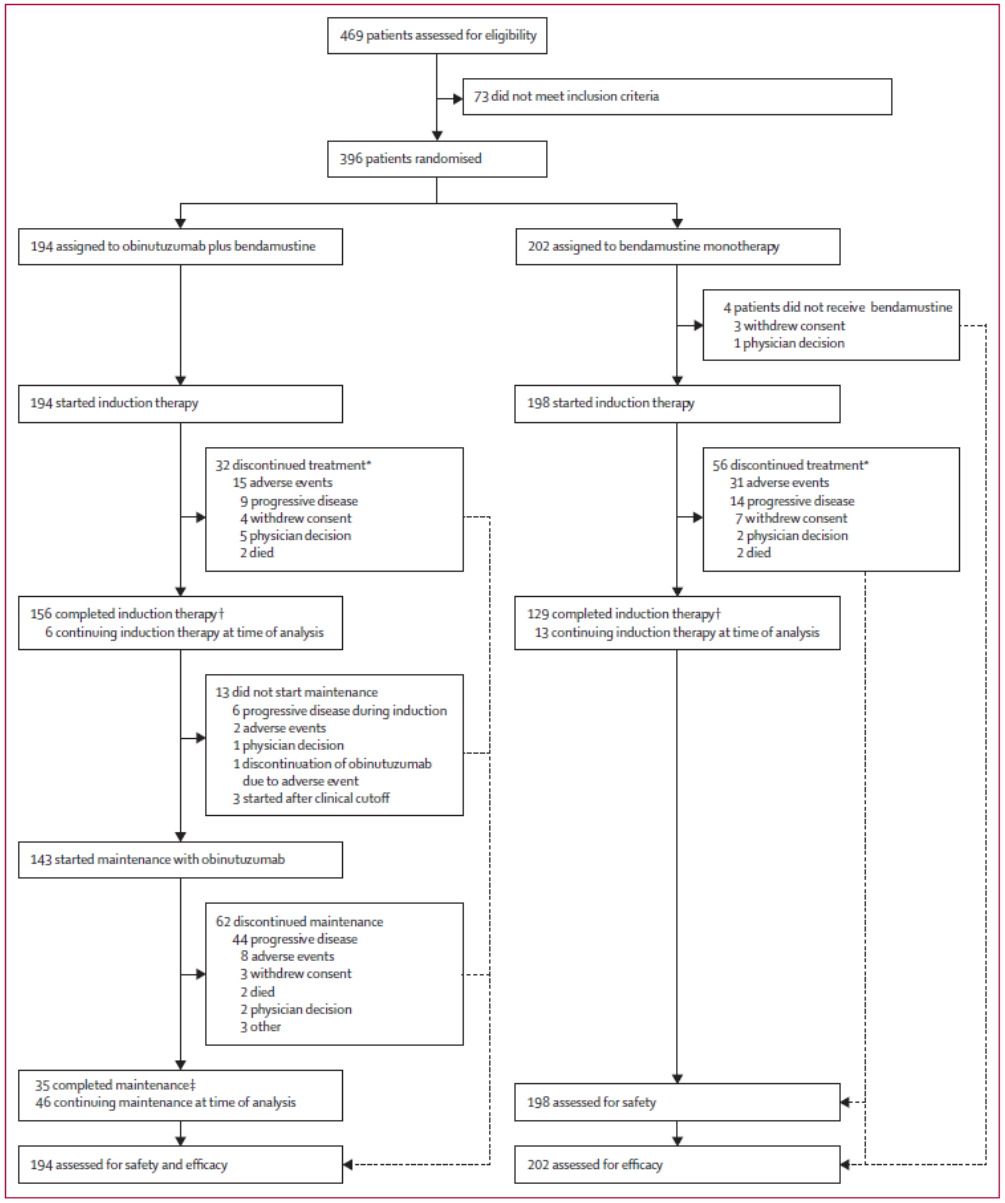


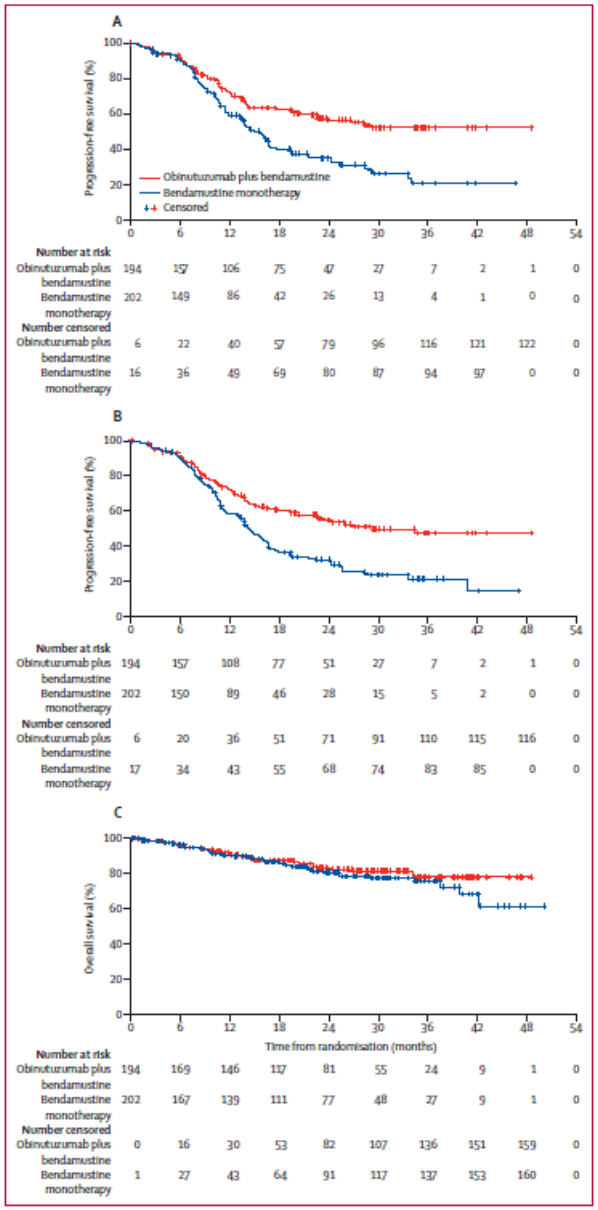
Figure 1: Trial profile

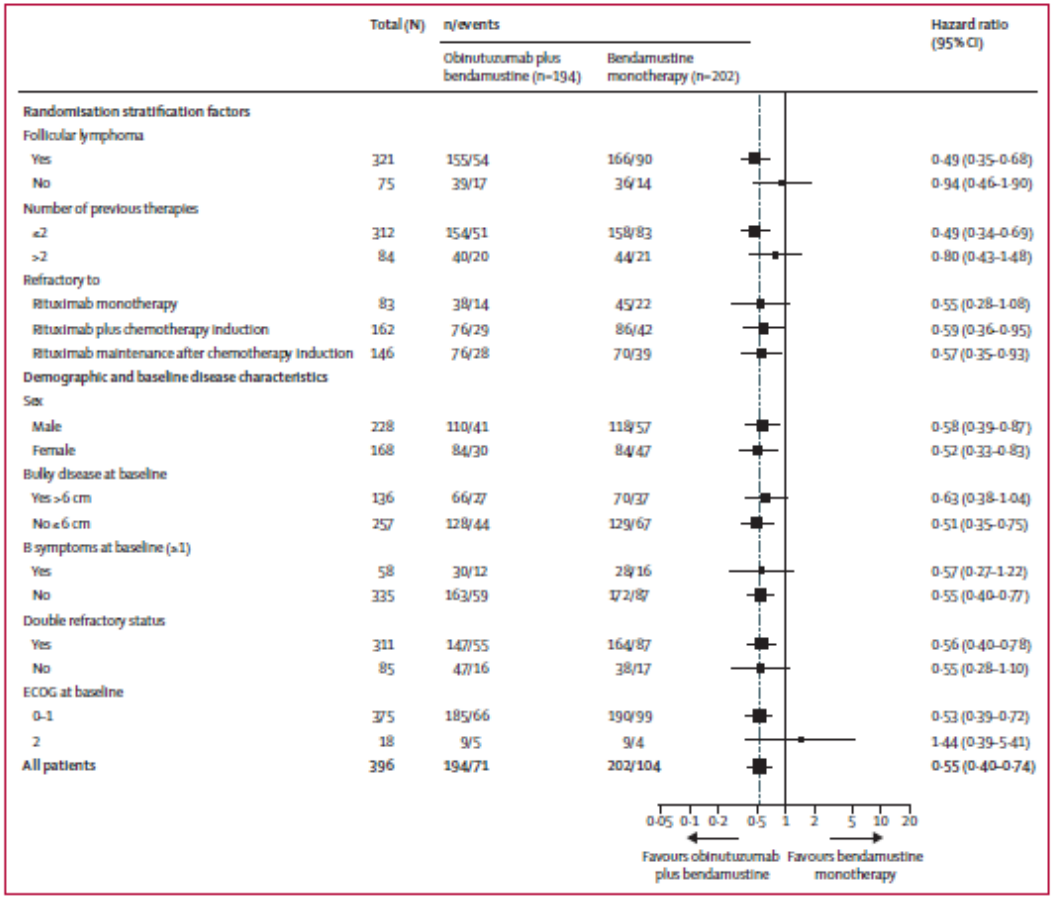
	Obinutuzumab plus bendamustine (n=194)	Bendamustine monotherapy (n=202)
(Continued from previous column)		
Rituximab-refractory type		
Rituximab plus chemotherapy	156 (80%)	157 (78%)
No response or progressive disease during or within 6 months after last rituximab induction dose	76/156 (49%)	86/157 (55%)
Progressive disease during or within 6 months after last rituximab maintenance dose	76/156 (49%)	70/157 (45%)
Other¶	4/156 (3%)	1/157 (1%)
Rituximab monotherapy	38 (20%)	45 (22%)

Data are n (%) or median (IQR), unless otherwise shown. INHL=indolent non-Hodgkin lymphoma. FLIPI=Follicular Lymphoma International Prognostic Index. *Patients not designated as grade 3a or 3b. †Status at initial diagnosis, for patients with follicular lymphoma only. ‡One patient had a negative value because of an incorrect treatment completion date. §Patients who were refractory to rituximab and alkylator agent in the same or separate regimens. ¶Patients who progressed more than 6 months after last rituximab dose but within 6 months after best response, and patients whose refractory status could not be classified because of insufficient detail in case report form.

Table 1: Baseline patient demographics and disease characteristics (intention-to-treat population)

Sehn L et al, Lancet 2016


A
Progression-free survival (%)
Obinutuzumab plus bendamustine
Bendamustine monotherapy
Censored
Number at risk
Obinutuzumab plus bendamustine 194 157 106 75 47 27 7 2 1 0
Bendamustine monotherapy 202 149 86 42 26 13 4 1 0 0
Number censored
Obinutuzumab plus bendamustine 6 22 40 57 79 96 116 121 122 0
Bendamustine monotherapy 16 36 49 69 80 87 94 97 0 0
B
Progression-free survival (%)
Number at risk
Obinutuzumab plus bendamustine 194 157 108 77 51 27 7 2 1 0
Bendamustine monotherapy 202 150 89 46 28 15 5 2 0 0
Number censored
Obinutuzumab plus bendamustine 6 20 36 51 71 91 110 115 116 0
Bendamustine monotherapy 17 34 43 55 68 74 83 85 0 0
C
Overall survival (%)
Time from randomisation (months)
Number at risk
Obinutuzumab plus bendamustine 194 169 146 117 81 55 24 9 1 0
Bendamustine monotherapy 202 167 139 111 77 48 27 9 1 0
Number censored
Obinutuzumab plus bendamustine 0 16 30 53 82 107 136 151 159 0
Bendamustine monotherapy 1 27 43 64 91 117 137 153 160 0


Total (N)
n/events
Obinutuzumab plus bendamustine (n=194)
Bendamustine monotherapy (n=202)
Hazard ratio (95% CI)
Randomisation stratification factors
Follicular lymphoma
Yes 321 155/54 166/90 0·49 (0·35–0·68)
No 75 39/17 36/14 0·94 (0·46–1·90)
Number of previous therapies
≤2 312 154/51 158/83 0·49 (0·34–0·69)
>2 84 40/20 44/21 0·80 (0·43–1·48)
Refractory to
Rituximab monotherapy 83 38/14 45/22 0·55 (0·28–1·08)
Rituximab plus chemotherapy induction 162 76/29 86/42 0·59 (0·36–0·95)
Rituximab maintenance after chemotherapy induction 146 76/28 70/39 0·57 (0·35–0·93)
Demographic and baseline disease characteristics
Sex
Male 228 110/41 118/57 0·58 (0·39–0·87)
Female 168 84/30 84/47 0·52 (0·33–0·83)
Bulky disease at baseline
Yes ≥6 cm 136 66/27 70/37 0·63 (0·38–1·04)
No <6 cm 257 128/44 129/67 0·51 (0·35–0·75)
B symptoms at baseline (≥1)
Yes 58 30/12 28/16 0·57 (0·27–1·22)
No 335 163/59 172/87 0·55 (0·40–0·77)
Double refractory status
Yes 311 147/55 164/87 0·56 (0·40–0·78)
No 85 47/16 38/17 0·55 (0·28–1·10)
ECOG at baseline
0–1 375 185/66 190/99 0·53 (0·39–0·72)
2 18 9/5 9/4 1·44 (0·39–5·41)
All patients 396 194/71 202/104 0·55 (0·40–0·74)
0·05 0·1 0·2 0·5 1 2 5 10 20
Favours obinutuzumab plus bendamustine
Favours bendamustine monotherapy

Trneny M et al S440
OBINUTUZUMAB PLUS BENDAMUSTINE VERSUS BENDAMUSTINE ALONE IN PATIENTS WITH RITUXIMAB-REFRACTORY FOLLICULAR LYMPHOMA: RESULTS FROM THE GADOLIN STUDY

BACKGROUND

FL subset analysis of GADOLIN pts. 321 (81%) of 396 iNHL pts enrolled had FL.

METHODS

Pts received either G + B90 or B120

RESULTS

Median number of prior therapies was 2. 94% pts were refractory to their last prior rituximab (R)-containing regimen and 88% double-refractory to R and an alkylating agent.

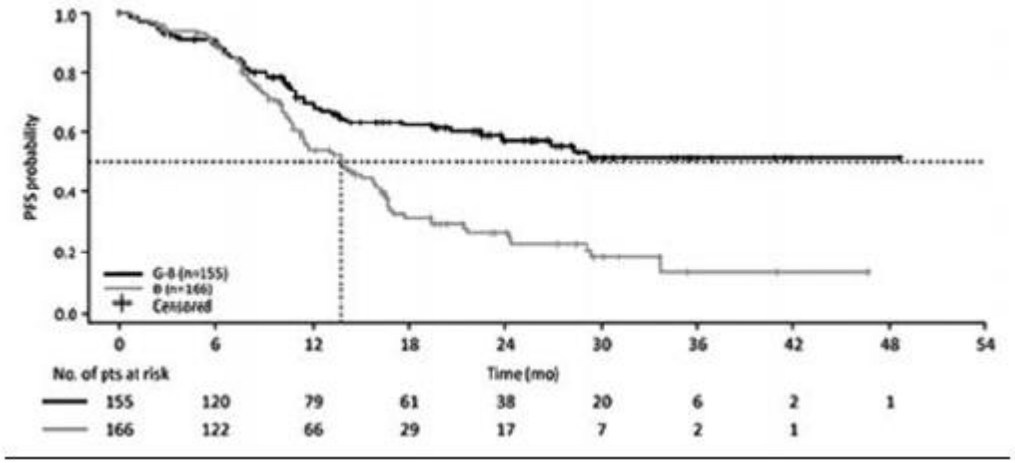
According to IRC PFS is not reached in the G-B arm and 13.8 mo in the B arm (Figure 1),

Survival data were immature at the time of analysis. Safety profiles were comparable.

Table 1.

Parameter	FL subpopulation	
	G-B (n=155)	**B (n=166)**
Median observation time (range), mo	22.08 (0.4-48.5)	20.27 (0.0-50.0)
PFS (IRC)		
Pts with event, n (%)	54 (34.8)	90 (54.2)
Median (mo)	Not reached	13.8
HR [95% CI]; stratified*	0.48 [0.34-0.68]	
PFS (INV)		
Pts with event, n (%)	62 (40.0)	102 (61.4)
Median (mo)	29.2	13.7
HR [95% CI]; stratified*	0.48 [0.35-0.67]	
Response† (IRC)		
EOI response (%): overall‡/CR	70.5/9.4	62.6/13.5
Best response (%): overall‡/CR	79.7/15.7	77.0/19.3

**Stratification factors for FL population were refractory type (R vs R-chemo) and prior therapies (≤2 vs >2); †During treatment and within 12 mo after start of treatment; ‡Complete response (CR) or partial response.*



ANALYSIS OF SECONDARY NEOPLASIAS AFTER HIGH DOSE THERAPY SUPPORTED BY AUTOLOGOUS STEM CELL TRANSPLANTATION IN FOLICULAR LYMPHOMA PATIENTS. A LONG TERM FOLLOW-UP ANALYSIS FROM THE GELTAMO REGISTRY.

BACKGROUND

- HDT/ASCTis effective in FL
- Secondary neoplasia is one the major cncern

To evaluate the cumulative incidence and characteristics of sMDS/sAML and solid tumors after HDT/ASCT in a very long-term follow-up analysis of FL patients.

METHODS

A total of 655 FL patients (GELTAMO registry)

RESULTS

Median follow-up 12 years. The median OS were 21.3 years from HDT/ASCT and 22.6 years from the time of FL diagnosis. 12.5% developed a second malignancy: solid tumors (47.5%), sMDS/sAML (42.5%). The accumulated incidence at 5, 10 and 15 years was 1.8%, 3.5% and 4.9% for solid tumors and 2.6%, 4.3% and 5% for sMDS/sAML. Male sex and BM as stem cell source were associated to an increased risk.

Characteristics		No.[a]	%
All patients		655	100
Median age, years (range)		47 (18-73)	
Sex: Male/ Female		330/ 325	50.4/ 49.6
FLIPI Score	Low	108	33
	Intermediate	120	36
	High	102	31
FLIPI 2 Score	Low	69	22
	Intermediate	118	38
	High	125	40
Disease Status at ASCT	CR	405	62
	PR	221	34
	Refractory disease	29	4
Anthracycline-containing first line therapy		460	76
Fludarabine-containing first line therapy		36	6
Only one therapy line before HDT/ASCT		183	28
Rituximab previous HDT, Yes/ No		184/ 436	30/ 70
Conditioning Regimen TBI based, Yes/ No		109/ 504	17/ 83
PBPC, Yes/ No		517/87	14.5/ 85.5

Abbreviations: BM: Bone Marrow, FLIPI: Follicular Lymphoma prognostic index, CR: Complete Response,PR: Partial Response, ASCT: Autologous Stem Cell Transplantation, HDT: High Dose Therapy, TBI: Total Body Irradiation, PBPC: Peripheral Blood Progenitor Cells.
a There are some missing data for several variables. No. of missing values can be directly derived for each variable by the equation: 655-(sum of available results)

CONCLUSIONS

FL pts are at an increased risk of second malignancy but not as high as reported.

Low percentage of TBI and early transplant could explain these good results.

Once a secondary neoplasia is diagnosed prognosis is dismal.

the incidence of secondary neoplasia will probably not diminish the benefit of HDT/ASCT in relapsed FL.

Hatake et al P686

INTERIM ANALYSIS OF POST MARKETING SURVEILLANCE OF YTTRIUM-90 IBRITUMOMAB TIUXETAN IN JAPANESE PATIENTS WITH RELAPSED OR REFRACTORY INDOLENT B-CELL NON-HODGKIN LYMPHOMA OR MANTLE CELL LYMPHOMA.

RESULTS

413 pts enrolled. Good safety confirmed.

ORR in 354 evaluable pts was 76.8%, CR rate 47.7%.

ORR and CR for those receiving 2 or less prior regimens were 86.0% and 56.1% respectively, while

ORR and CR for those receiving more than 2 prior regimens were 69.3% and 40.7%

CONCLUSIONS

90YITis a tolerable and efficacious treatment option for pts with R/R B-cell NHL or MCL in Japan,

It demonstrates good benefit-risk balance

Li JJ et al P317
IDELALISIB MONOTHERAPY IN RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL): EXPERIENCE THROUGH AN EARLY ACCESS PROGRAM IN EUROPE AND AUSTRALIA

Baseline Demography	Total (n=66)
FL Grade, n (%)	
1	9 (14.1)
2	32 (50)
3a	23 (35.9)
Documented	64
Missing data	2
Age, years	
Median, (range)*	66 (40-86)
Male*, n (%)	32 (48.5)
Ann Arbor stage at enrollment, n (%)	
I	2 (3.0)
II	4 (6.1)
III	19 (28.8)
IV	41 (62.1)
High risk FLIPI-2 score at enrollment, n (%)	39 (63.9)
Documented	61
Missing data	5
ECOG, n (%)	
0	24 (36.4)
1	32 (48.5)
2	10 (15.2)
3	0
Number of prior regimens, median (range)	4 (2-13)

RESULTS Results: 66 pts with refractory FL who had documented prior treatment regimens. A total of 12 pts (20%) ASCT .

With a median follow up of 109 days IDELA monotherapy was well-tolerated with 6/66 pts (9.1%) reporting an SAE.

(Febrile neutropenia, neutropenia, diarrhea, gastrointestinal inflammatory disorder, pancytopenia, progressive disease, liver enzyme elevation, hypotension and colon cancer).

CONCLUSIONS: The results confirm the acceptable tolerability profile of IDELA.

THREE QUESTIONS TO ADDRESS:

1. **Is ASCT still the golden standard for MCL? And how to challenge it in the future?**
2. **What is new in relapsed follicular lymphoma? Is benda-obinotuzumab a major step forward? Which are the alternatives?**
3. **Ultra high-risk lymphoma patients: Can we identify them? And where shall we go for treatment?**

Casasnovas O et al S105

BASELINE TOTAL METABOLIC VOLUME (TMTV) PREDICTS THE OUTCOME OF PATIENTS WITH ADVANCED HODGKIN LYMPHOMA (HL) ENROLLED IN THE AHL2011 LYSA TRIAL.

BACKGROUND

The TMTV assessed on the baseline FDG-PET assessed prospectively in pts enrolled in a phase III randomized trial (PET-driven)

RESULTS

- follow-up of 16 months, 2y-PFS was 81% vs 93% in pts with high and low TMTV

- Using also PET-2 3 groups could be identified having a 61%, 88%, 94% 2y-PFS respectively ($p<0.0001$).

CONCLUSIONS

The TMTV predicts the outcome of young advanced HL pts. The combination of TMTV and PET2 allows identifying 3 subsets of HL pts

Stewart D et al S479
A BIOCLINICAL PROGNOSTIC MODEL INCORPORATING MYC AND BCL2 PREDICTS OUTCOME TO SALVAGE THERAPY IN RELAPSED/ REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: AN NCIC CTG LY12 CORRELATIVE SCIENCE STUDY.

BACKGROUND

To determine clinical and molecular predictors of EFS and OS for rrDLBCL pts treated with R-GDP or R-DHAP followed by ASCT (Canadian Ly12 study)

METHODS

91 pts had DLBCL immunohistochemical (IHC) testing for CD10, BCL6, MUM1, FOXP1, LMO2, BCL2, CMYC, P53, pySTAT3 expression.

In addition, 97 formalin-fixed, had GEP with NanoString to evaluate Cell of Origin (COO) by the Lymph2Cx assay, as well as BCL2, MYC, P53, STAT3, PDL1 and PD1 expression.

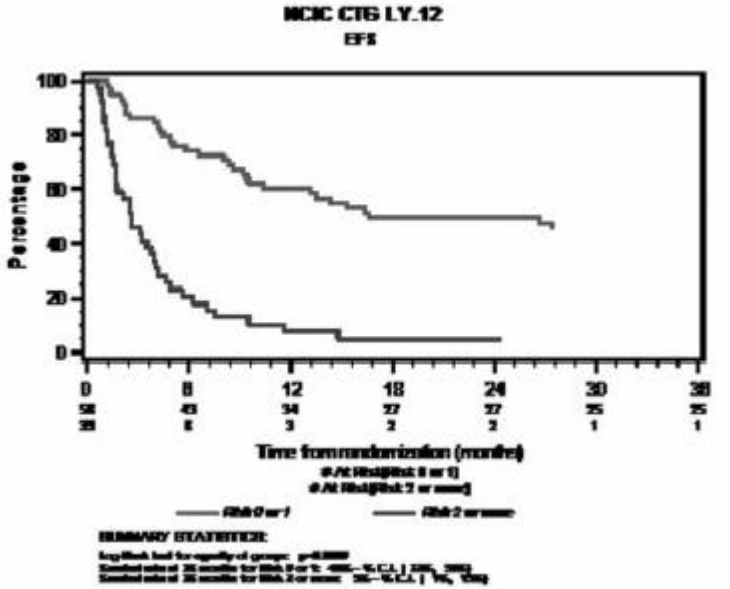
RESULTS

- **Expression of both MYC and BCL2 was associated to poor outcome**. Dual expressing (DE) lymphomas (MYC+/BCL+) had significantly worse 3y EFS (0% vs 40%, p=0.0009) and OS rates (20% vs 54%, p=0.0004)

Stewart D et al S479
A BIOCLINICAL PROGNOSTIC MODEL INCORPORATING MYC AND BCL2 PREDICTS OUTCOME TO SALVAGE THERAPY IN RELAPSED/ REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: AN NCIC CTG LY12 CORRELATIVE SCIENCE STUDY.

MYC and BCL2 expression using NanoString GEP (>1.5xmean) were significantly associated with inferior OS and EFS, and no patient who expressed both markers achieved 2y EFS or OS.

Concordance rate of 79% was seen for MYC and 57% for BCL2. In multivariate analyses, primary refractory DLBCL, LDH at relapse, MYC expression and BCL2 expression (assessed by either IHC or GEP).



CONCLUSIONS

MYC and BCL2 expression, determined by IHC or Nanostring GEP, are independent poor prognostic factors for rrDLBCL, and dual expression predicts dismal prognosis.

Tchernonog E et al S788

CLINICAL CHARACTERISTICS AND PROGNOSTIC FACTORS OF IMMUNOCOMPROMISED AND NON IMMUNOCOMPROMISED PLASMABLASTIC LYMPHOMA PATIENTS: ANALYSIS OF 135 PATIENTS TREATED IN THE LYSA GROUP.

BACKGROUND

PBL remains a diagnostic and therapeutic challenge with an aggressive clinical course. Aim of this study was to specify the clinical, biological, pathological features and outcome of patients with PBL.

METHODS AND RESULTS

135 patients with PBL diagnosed after 2000 within LYSA. The median age was 58, male predominance. 56 HIV-positive patients, 17 post-transplant patients, and 62 "immunocompetent".

However also this subtype of patients may present some degree of immunodepression.

Immunophenotype showed CD138 positivity in 88% of cases and CD20 negativity in 90% of cases. EBER expression was observed in 62% of cases**. Chemotherapy was administered to 108 of 135 patients, with a complete response rate of 55%.**
Rituximab, had a trend towards improved CR rate. The median overall survival was 32 mos. HIV positive status showed better overall survival.

DISCUSSION

Specific guidelines to clarify all the treatment options are lacking

Festuccia M et al 796

ALLOGENEIC STEM CELL TRANSPLANTATION AND BRENTUXIMAB VEDOTIN IN RELAPSED/REFRACTORY HODGKIN LYMPHOMA: A MULTICENTER EXPERIENCE

BACKGROUND

allo-HCT has been used in RR HL with controversial results. Aim of our study is to investigate the role of allo-HCT in RR HL

METHODS

69 patients with RR HL, median age 34 (range, 18 - 64), **52 patients (75%) were at least in PR.** The remaining **16 patients (23%) had progressive disease** (non-responsive).

Brentuximab Vedotin (BV) was given as bridge to transplant in 11 patients. Moreover, 7 patients received BV after allo-HCT.

The majority of patients underwent reduced intensity allo-HCT, 64 patients (93%). MUD in 57%. The stem cells source was PB in 61 patients (88%).

RESULTS

Median OS of 5.1 years (range, 0 - 13.8) and RFS of , 1.3 years.

The 5-year cumulative incidence of treatment related mortality (TRM) and relapse were 17.7% and 43.4%, respectively.

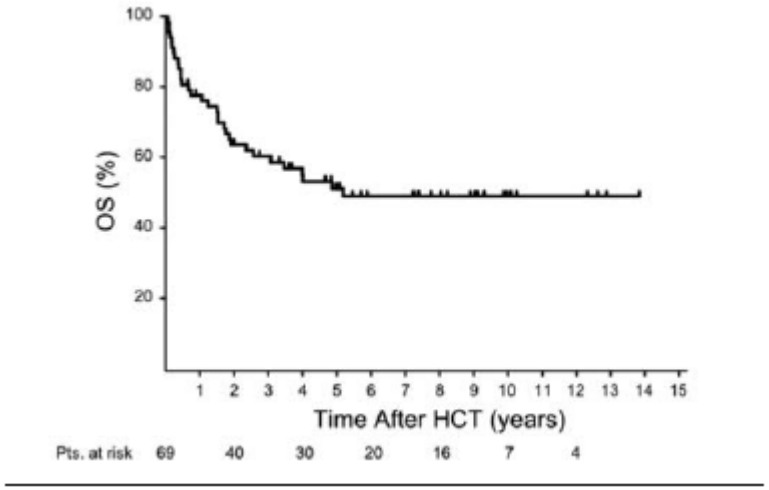
The 5-year estimated of RFS was significantly higher in responsive compared to non-responsive patients, 46.9% versus 12.5%, respectively, p= 0.009.

Eleven patients received BV as bridge to allo-HCT for a median of 6 cycles.. All patients achieved at least PR. None of patients treated with BV had unexpected toxicity or GVHD worsening.

DISCUSSION

Allo-HCT is a feasible and effective option for RR HL.

BV showed efficacy as a bridge to allo- HCT as well as post allo-HCT rescue.



CHALLENGING HIGH-RISK PATIENTS

TRADITIONAL BACKBONE TREATMENT

Poor diagnostic profile

Failure to achieve MRD/PET negativity or MRD loss

Innovative or potentiated treatment

THANK YOU FOR YOUR ATTENTION!!!!

HAVE AN EXCITING AND FRUITFUL DISCUSSION !!!!

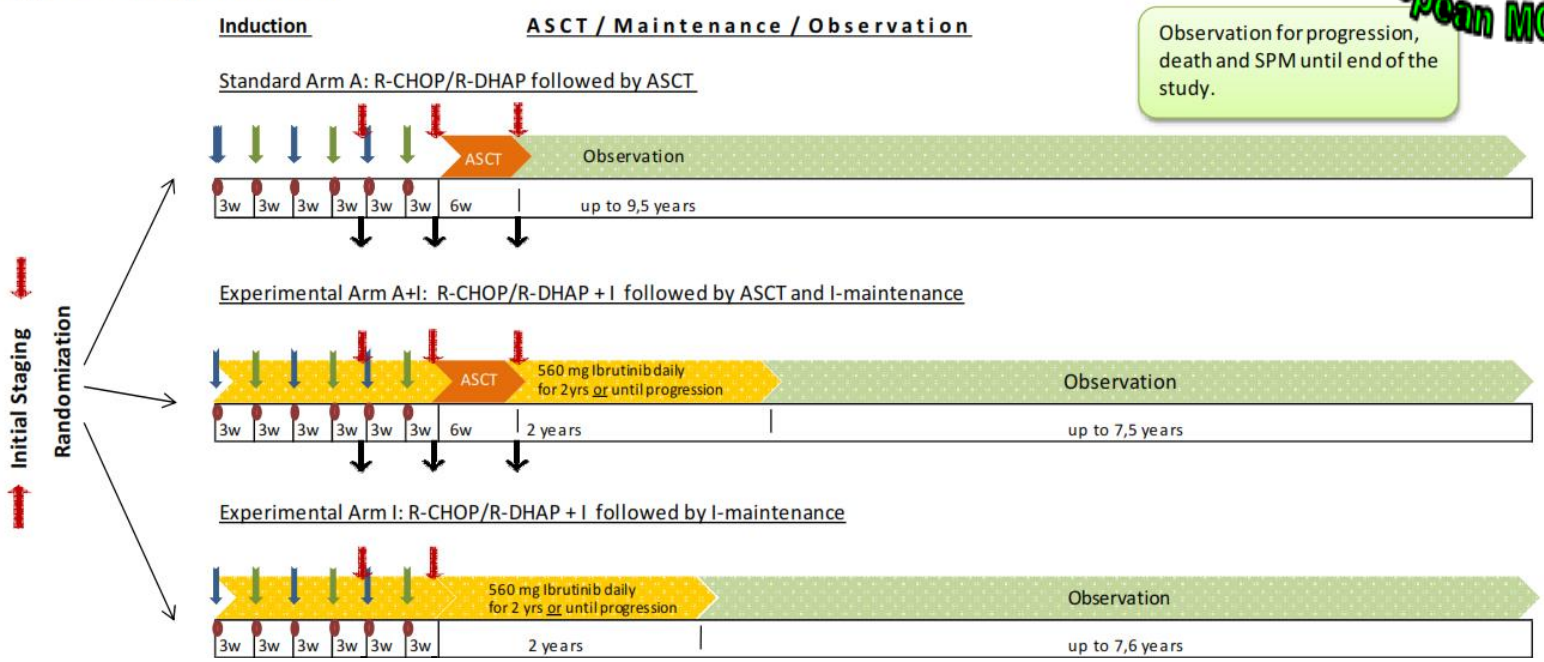
Azienda Ospedaliera Nazionale
SS. Antonio e Biagio e Cesare Arrigo
Alessandria

FONDAZIONE FIL ITALIANA LINFOMI

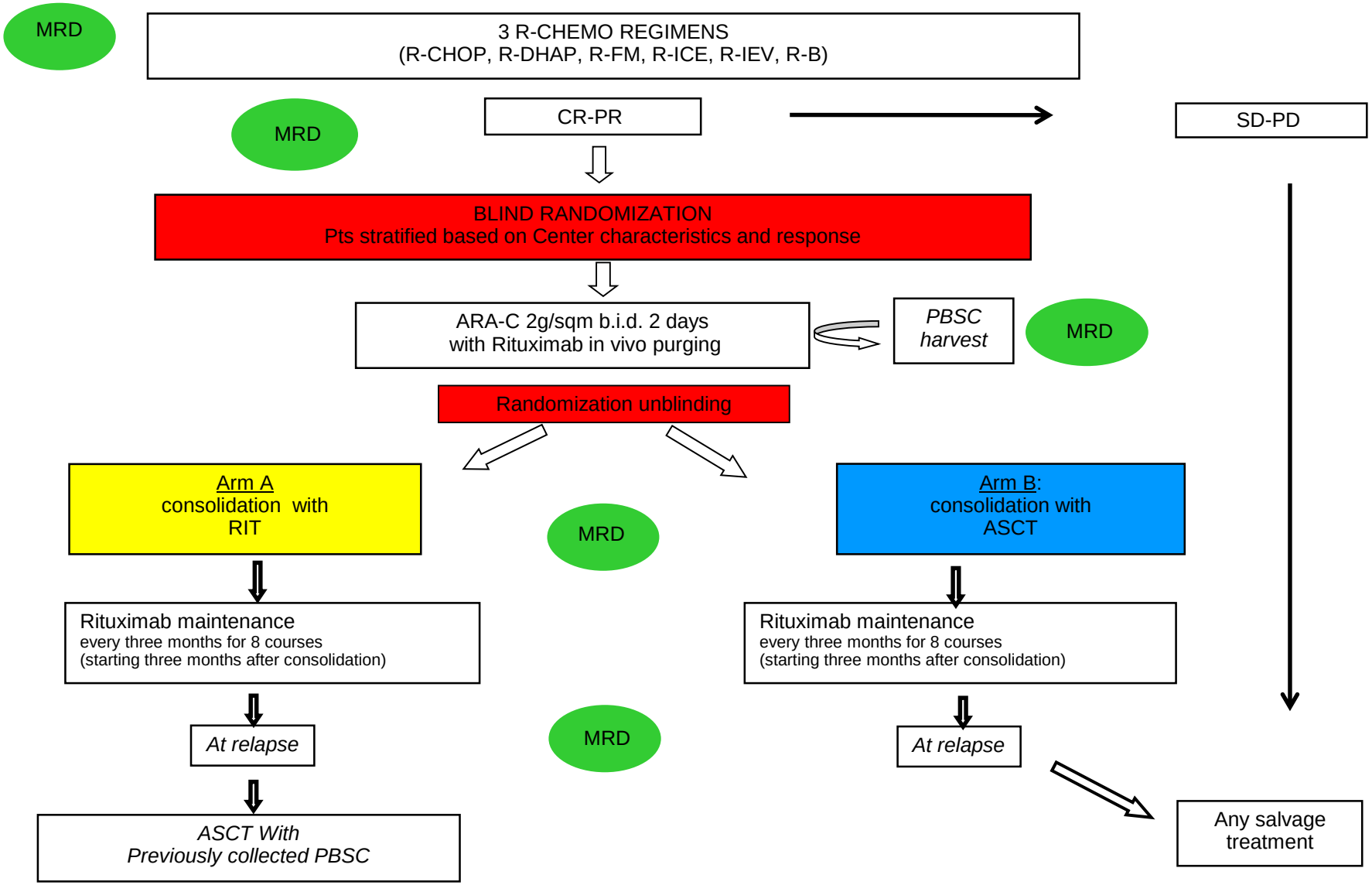
European MCL Network

TRIANGLE study
Flow chart

Figure 2: Study flow chart



FLAZ-12: STUDY DESIGN



rotocols in relapsed FL: Renoir

A randomized phase III multicenter trial assessing efficacy and toxicity of a combination of Rituximab and Lenalidomide (R2) vs Rituximab alone as maintenance after chemoimmunotherapy with Rituximab-Bendamustine for relapsed/refractory FL patients not eligible for autologous transplantation (ASCT).

RELAPSED/REFRACTORY
FOLLICULAR LYMPHOMA
NEED TO THERAPY

R-Bendamustine x 4 once a month

Rituximab 375 mg/m^2 day 0 or 1 (day 8 on cycle 1)
Bendamustine 90 mg/m^2 iv days 1-2

CR/PR → NR → OFF

Random

R2

Rituximab 375 mg/m2 day 1 q 90 days (8 cycles)
Lenalidomide (10 mg dd 1-21 q 28) (24 cycles)

R alone

Rituximab 375 mg/m2 day 1 q 90 days (8 cycles)