Frankfurt 22. – 23.März 2019

Hämatologie im Wandel

Indolente Lymphome – Behandlungsstrategien und Studien der GLA

C. Buske
CCC Ulm
Klinik für Innere Medizin III
Universitätsklinikum Ulm

Integratives Tumorzentrum des Universitätsklinikums und der Medizinischen Fakultät
Comprehensive Cancer Center Ulm

ulm university universität ulm

AG Indolente Lymphome

German Lymphoma Alliance (GLA)

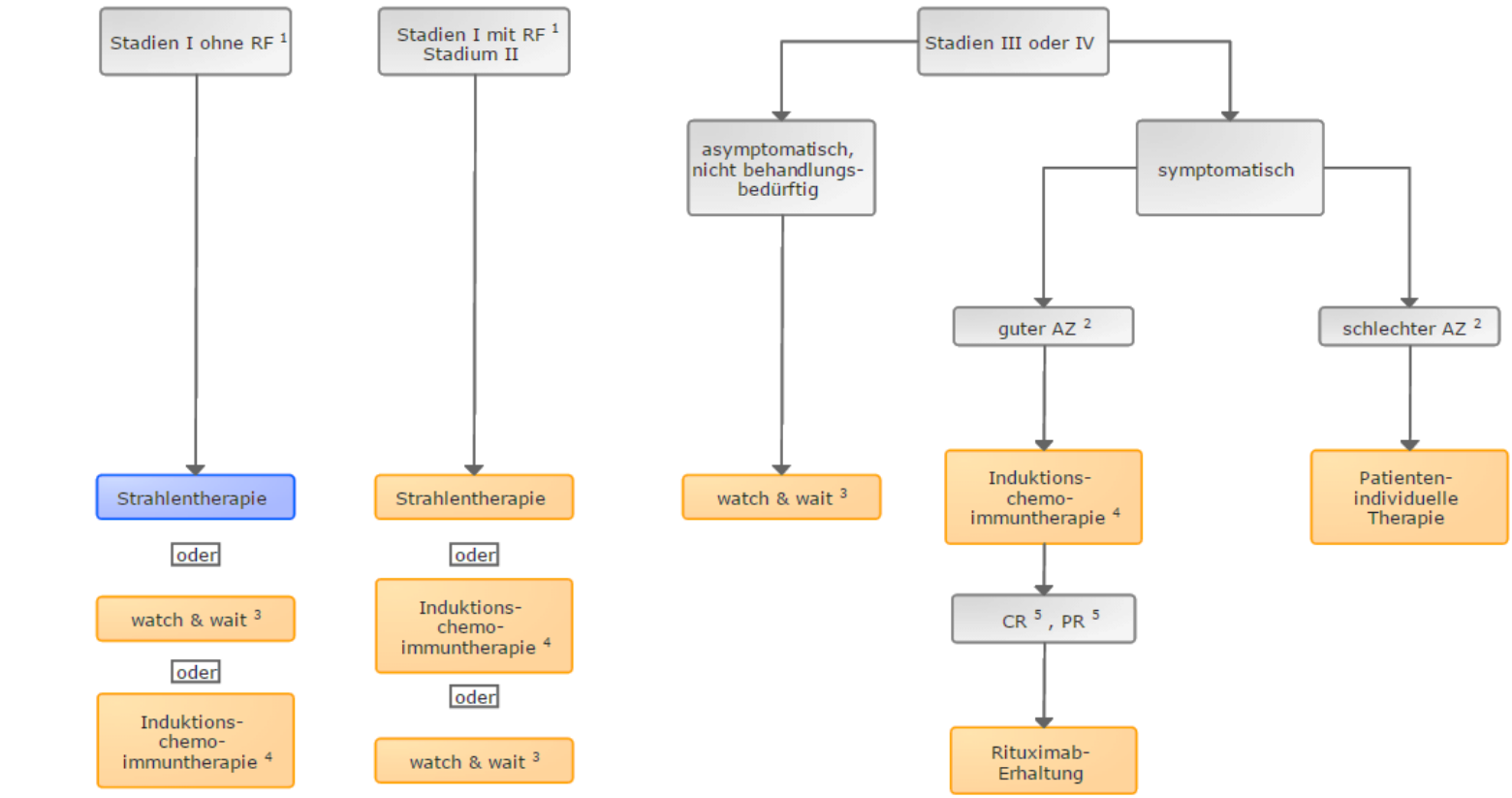
Gründungstreffen März 2017, Frankfurt

Indolente B - NHL

1. **Follikuläres Lymphom (fortgeschrittene Lymphome)**
2. Morbus Waldenström
3. Marginalzonenlymphom

Therapeutischer Algorithmus – Leitlinien der DGHO

Abbildung 1: Erstlinientherapie des Follikulären Lymphoms



Legende: *kurative Therapieintention;* *palliative Therapieintention;*

[1] *RF – Risikofaktoren (LK ≥ 5 cm)*

[2] *AZ - Allgemeinzustand;*

[3] *watch & wait – abwartendes Verhalten unter regelmäßiger Beobachtung*

[4] *Induktionschemotherapie: R-Ben – Rituximab / Bendamustin oder R-CHOP – Rituximab / Cyclophosphamid / Doxorubicin / Vincristin / Prednison oder R-MCP – Rituximab / Mitoxantron / Chlorambucil / Prednison;*

[5] *CR – komplette Remission, PR – partielle Remission*

Buske et al., 2017

Comment on Flinn et al, page 3406; and Kahl et al, page 3398; and Brown et al, page 3390

CLL and NHL: the end of chemotherapy?

Bruce D. Cheson GEORGETOWN UNIVERSITY HOSPITAL

"The times they are a changin'"—Bob Dylan

Indolente Lymphome

Unser Ziel: „chemofreie" Ansätze

Comment on Flinn et al, page 3406; and Kahl et al, page 3398; and Brown et al, page 3390

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Unser Ziel: „chemofreie" Ansätze

Obinutuzumab Monotherapie ausreichend?

EudraCT-Nr.:
2016-000755-27

Sponsor: Klinikum der
Universität München

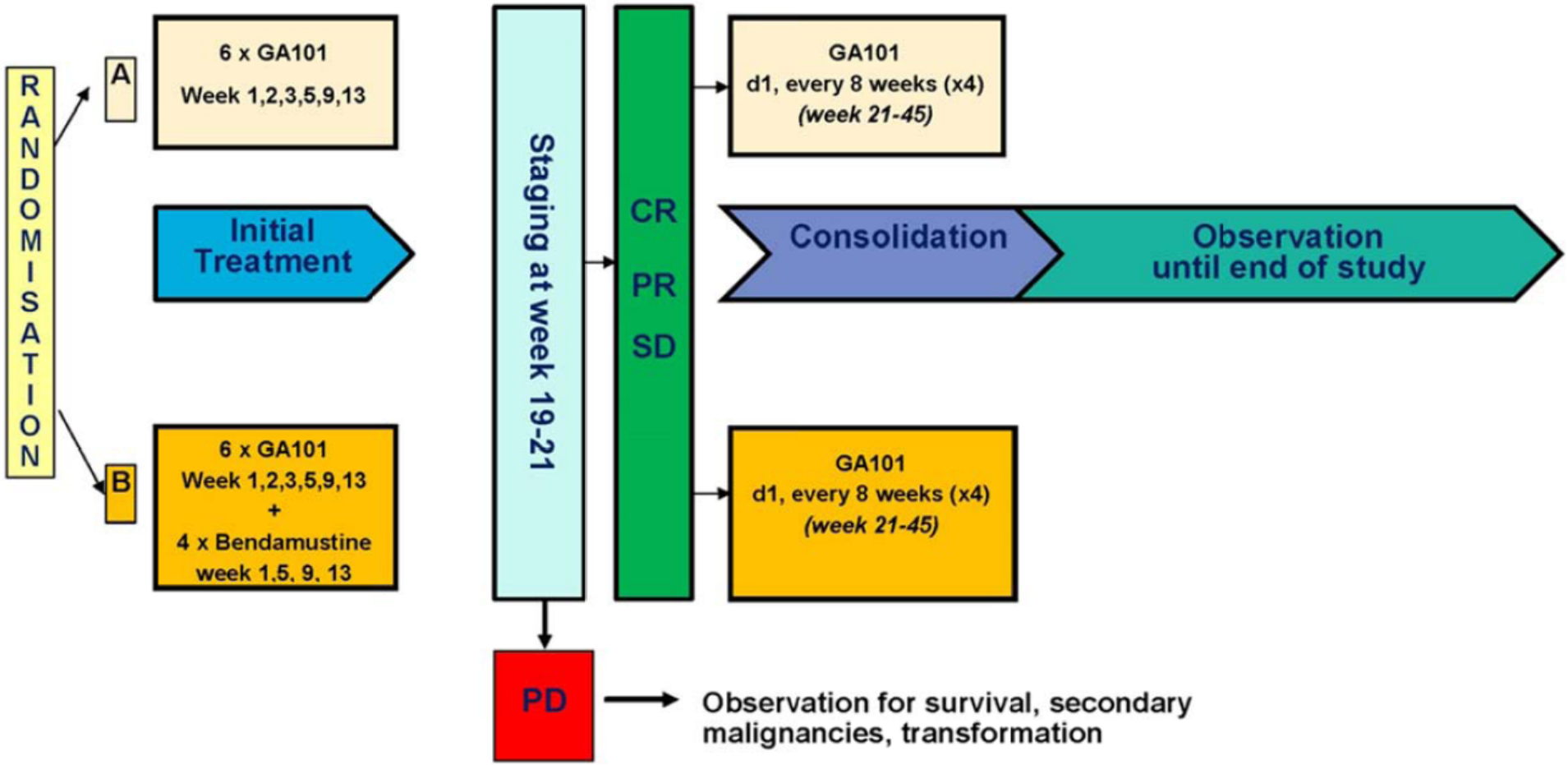
Intergroup-Study
of the GLSG/OSHO

FIRST LINE THERAPY OF ADVANCED STAGE FOLLICULAR LYMPHOMA IN PATIENTS NOT ELIGIBLE FOR STANDARD IMMUNOCHEMOTHERAPY

Prospective randomized comparison of single agent GA101 versus GA101 plus Bendamustine followed by GA101 in medically non-fit patients

-GABE 2016-

Trial Flow


RANDOMISATION
A
6 x GA101
Week 1,2,3,5,9,13
Initial Treatment
B
6 x GA101
Week 1,2,3,5,9,13
+
4 x Bendamustine
week 1,5, 9, 13
Staging at week 19-21
CR
PR
SD
GA101
d1, every 8 weeks (x4)
(week 21-45)
Consolidation
Observation
until end of study
GA101
d1, every 8 weeks (x4)
(week 21-45)
PD
Observation for survival, secondary
malignancies, transformation

Amendment geplant:

für alle Patienten 60 Jahre und älter!

FIRST LINE THERAPY OF ADVANCED STAGE FOLLICULAR LYMPHOMA
IN PATIENTS NOT ELIGIBLE FOR
STANDARD IMMUNOCHEMOTHERAPY

Prospective randomized comparison of single agent GA101 versus GA101 plus Bendamustine followed by GA101 in medically non-fit patients

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Unser Ziel: „chemofreie" Ansätze

Ibrutinib?

ALTERNATIVE

A prospective multicenter Phase 2 Study of the Chemotherapy-free Combination of the Bruton's Tyrosine Kinase Inhibitor, PCI-32765 (Ibrutinib) in Combination with Obinutuzumab (GA 101) in Patients with Previously Untreated Follicular Lymphoma (FL) and a High Tumor Burden

TREATMENT

6 cycles
Ibrutinib 560mg +
Obinutuzumab
1000mg

MAINTENANCE TREATMENT

Ibrutinib 560mg/d
+ Obinutuzumab
1000mg q8w
(for 2 years)

MRD-BASED MAINTENANCE

1 year additional
Ibrutinib treatment
for patients
remaining MRD-
positive after
maintenance

TIMELINE

First patient in:
Apr 2016
End of recruitment
May 2017
Primary Endpoint
May 2018
End of follow up
Dec. 2022

Comment on Flinn et al, page 3406; and Kahl et al, page 3398; and Brown et al, page 3390

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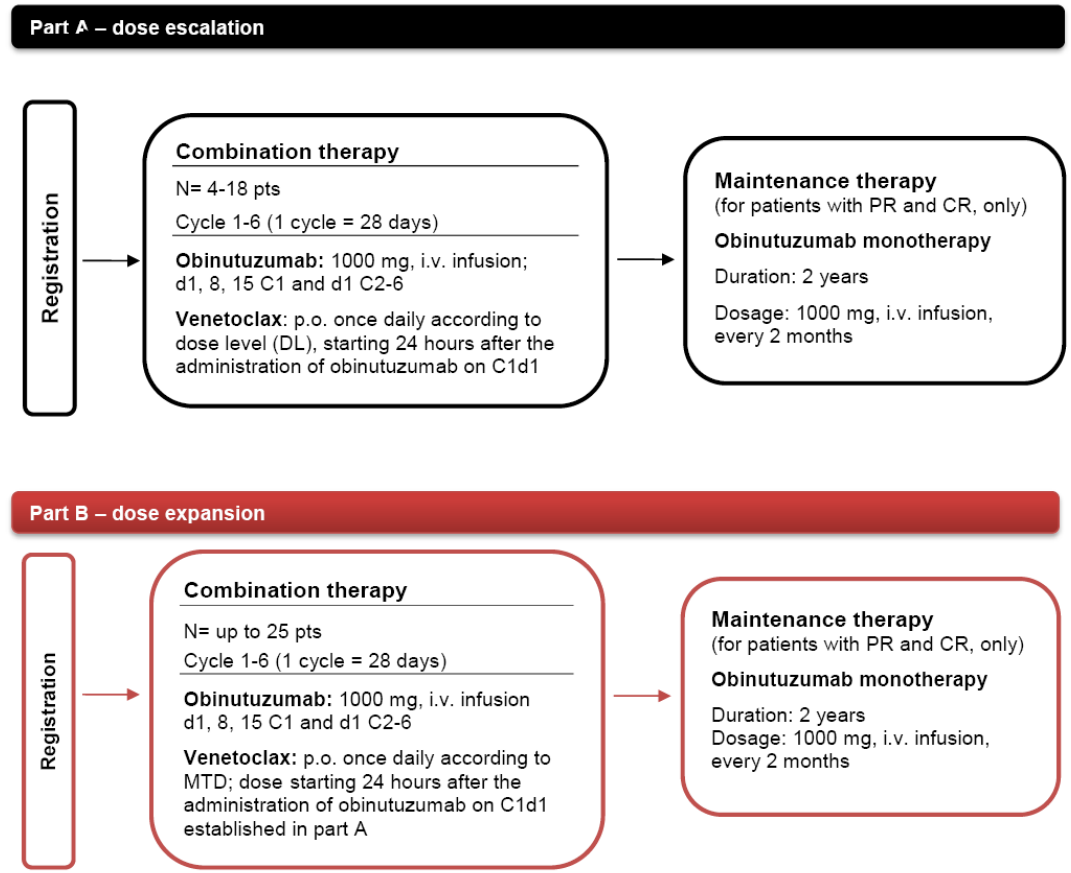
Indolente Lymphome
Unser Ziel: „chemofreie" Ansätze

Venetoclax?

Protocol SAKK 35/15

A phase I trial of obinutuzumab in combination with venetoclax in previously untreated follicular lymphoma patients



Indolente B - NHL

1. **Follikuläres Lymphom (fortgeschrittene Lymphome)**
2. **Morbus Waldenström**
3. Marginalzonenlymphom

European Consortium for Waldenström's Macroglobulinemia
ECWM - Trials 2018/19

Trials First Line

ECWM-1 (Phase III)
DRC versus Bortezomib-DRC
European, over 60 centers

ECWM-2 (Phase II)
Bortezomib-Rituximab/Ibrutinib
European
30 centers

CZAR-1 (ECWM-3 (Phase III)
Carfilzomib/Ibrutinib vs Ibrutinib
European
60 centers

Relapse

CZAR-1 (ECWM-3) (Phase III)
Carfilzomib/Ibrutinib vs Ibrutinib
European
60 centers

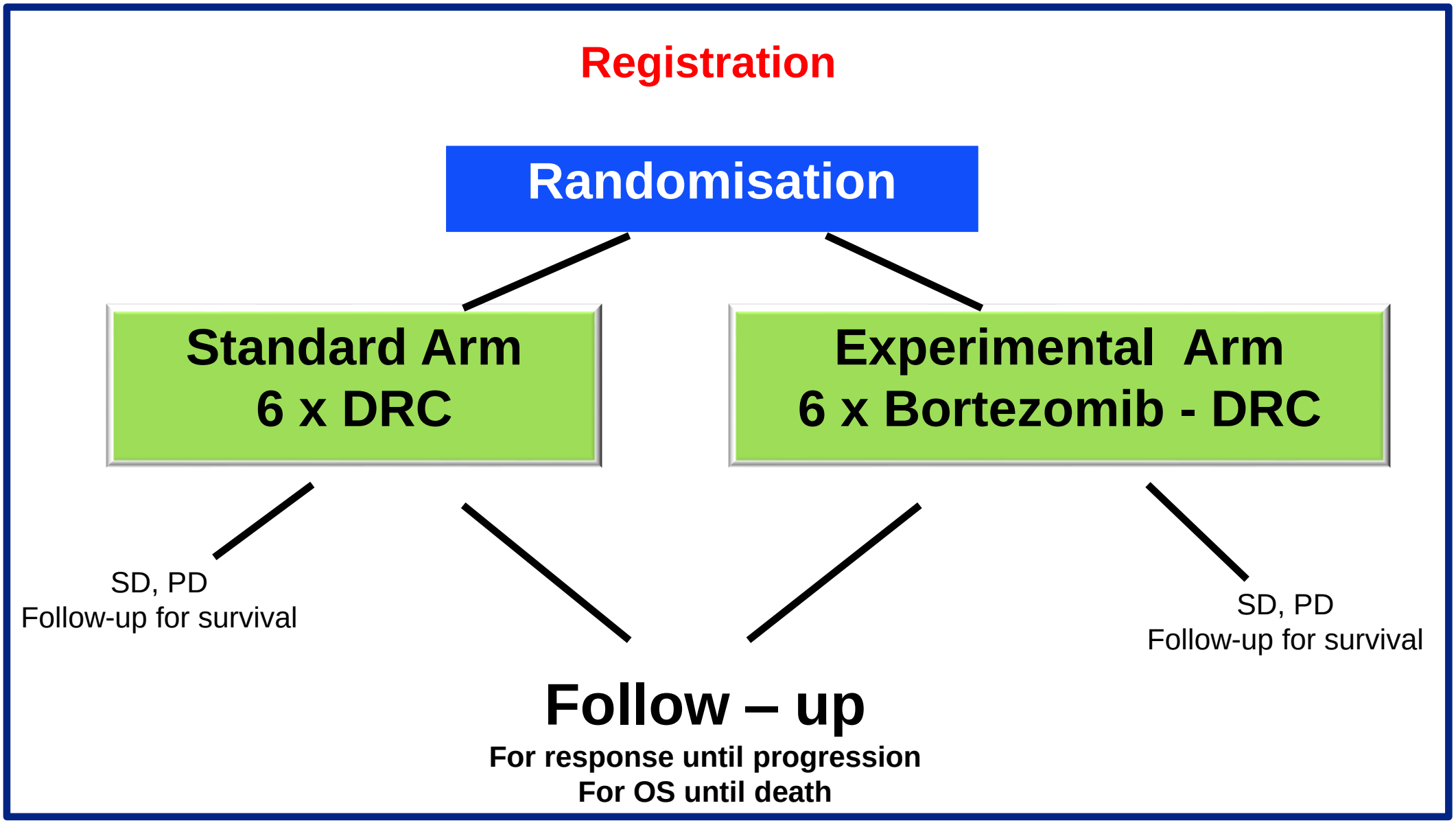
ECWM-R2 Phase II; Hovon, Greece
Ixazomib/Rituximab/Dex

ECWM-R3 Phase II; France
Idelalisib/GA101

http://www.ecwm.eu/clinical_trials/__Clinical-Trials.html

ECWM-1

first line WM



Study ECWM-1 - Status

- Study activated in: Germany, France, Greece, Sweden, Czech Republic, Spain, Portugal
- Patients randomized: 202, recuitment stopped
- Last patient included: Sept 2018
- Last patient off treatment: April 9 2019 scheduled

Comment on Flinn et al, page 3406; and Kahl et al, page 3398; and Brown et al, page 3390

CLL and NHL: the end of chemotherapy?

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Unser Ziel: „chemofreie" Ansätze

Waldenström's Macroglobulinemia

What about Ibrutinib?

What can we achieve (and what not) with Ibrutinib?

Ibrutinib as the most efficient single chemofree agent in WM

Waldenström's Macroglobulinemia

What about Ibrutinib?

What can we achieve (and what not) with Ibrutinib?

Challenges!

Responses to ibrutinib are impacted by MYD88 (L265P and non-L265P) and CXCR4 mutations

	$MYD88^{MUT}$ $CXCR4^{WT}$	$MYD88^{MUT}$ $CXCR4^{WHIM}$	$MYD88^{WT}$ $CXCR4^{WT}$	p-value
N=	36	21	5	
Overall RR	100%	85.7%	60%	<0.01
Major RR	91.7%	61.9%	0%	<0.01

2 patients subsequently found to have other MYD88 mutations not picked up by AS-PCR

Treon et al, N Engl J Med. 2015; 372(15):1430-40; NEJM 2015; Letter, August 6, 2015.

CXCR4 mutated and MYD88^{WT}/CXCR4^{WT} patients are „high risk“ patients in the era of ibrutinib

Approaches to improve on this!

Treatment of WM

What comes next?

Improving Ibrutinib (Ibrutinib as a backbone)!

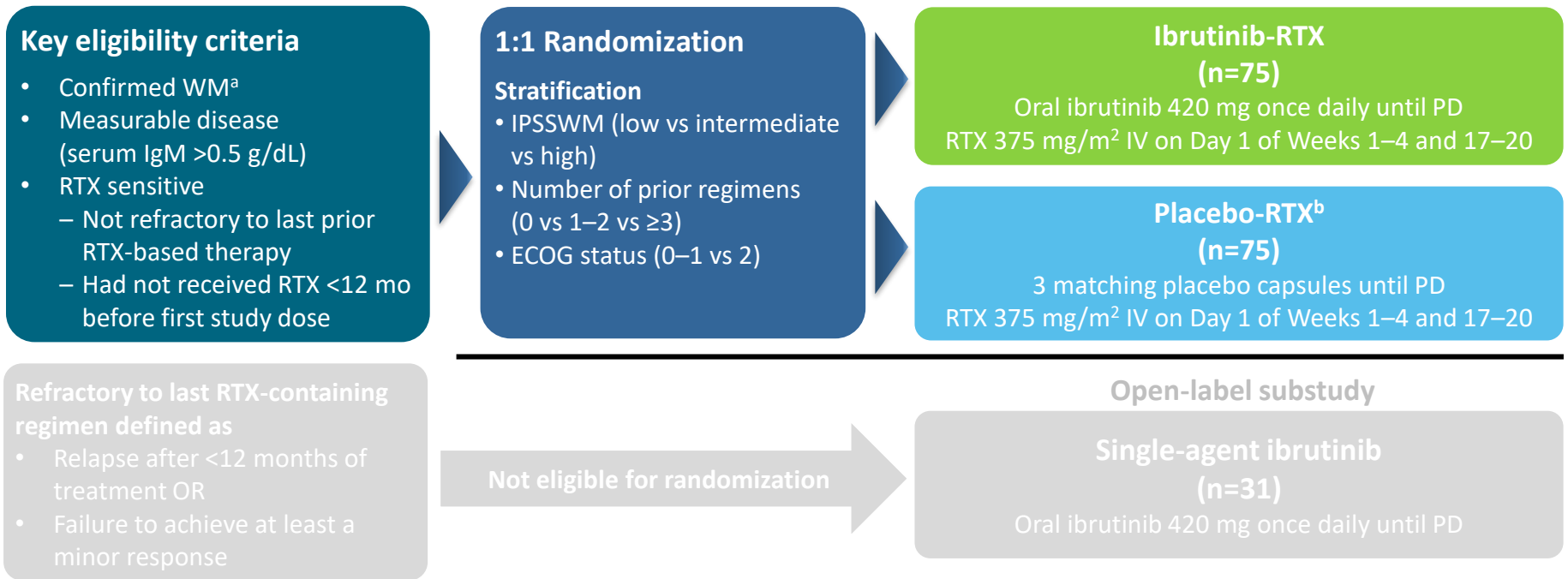
→ ***Rituximab/Ibrutinib?***
→ ***Ibrutinib/Proteasome inhibitor?***

Ibrutinib Treatment in Waldenström's Macroglobulinemia: Follow-up Efficacy and Safety from the iNNOVATE™ Study

Christian Buske, MD[1], Alessandra Tedeschi, MD[2], Judith Trotman, FRACP[3], Ramón García-Sanz, MD, PhD[4], David MacDonald, MD[5], Veronique Leblond, MD, PhD[6], Beatrice Mahe, MD[7], Charles Herbaux, MD[8], Constantine Tam, MD[9], M. Lia Palomba, MD[10], Jeffrey V. Matous, MD[11], Chaim Shustik, MD[12], Efstathios Kastritis, MD[13], Steven P. Treon, MD, PhD[14], Chih-Jian Lih, PhD[15], Jianling Li, MS[15], Zeena Salman, BS[15], Thorsten Graef, MD, PhD[15], Meletios A. Dimopoulos, MD[13] on behalf of the iNNOVATE Study Group and the European Consortium for Waldenström's Macroglobulinemia

[1]Comprehensive Cancer Center Ulm, Institute of Experimental Cancer Research, University Hospital of Ulm, Ulm, Germany;
[2]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [3]Concord Hospital, University of Sydney, Concord, Australia;
[4]Hospital Universitario de Salamanca, Salamanca, Spain; [5]The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada;
[6]Département d' Hématologie Hôpital Pitié-Salpêtrière APHP, UPMC Université Paris, Paris, France; [7]Centre Hospitalier Universitaire de Nantes, Nantes, France;
[8]Centre Hospitalier Régional Universitaire de Lille, Institute of Hematolog-Tranfusion, Lille, France;
[9]Peter MacCallum Cancer Centre & St. Vincent's Hospital and the University of Melbourne, Melbourne, Australia;
[10]Memorial Sloan Kettering Cancer Center, New York City, NY, USA; [11]Colorado Blood Cancer Institute, Denver, CO, USA;
[12]Royal Victoria Hospital at McGill University Health Centre, Montreal, Canada;
[13]National and Kapodistrian University of Athens School of Medicine, Athens, Greece;
[14]Dana-Farber Cancer Institute, Boston, MA, USA; [15]Pharmacyclics LLC, an AbbVie Company, Sunnyvale, CA, USA.

Randomized Study: iNNOVATE (PCYC-1127) Study Design

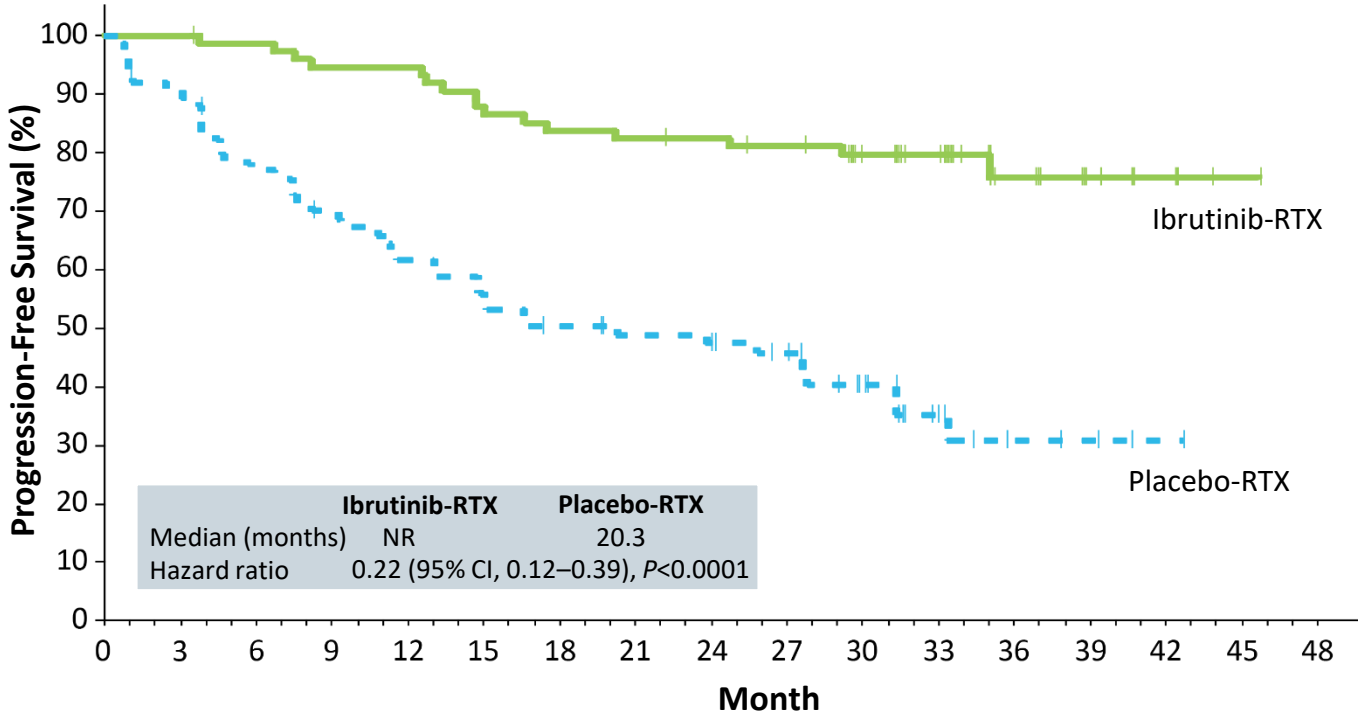


- **Primary endpoint:** PFS by IRC
- **Secondary endpoints** include response rate, OS, safety

[a]Treatment-naïve patients were allowed to enroll following a protocol amendment (Nov 2015); therefore, their enrollment started later than previously treated patients.
[b]Access to next-line ibrutinib (crossover) for patients treated with placebo in combination with rituximab may be provided after confirmed disease progression (by IRC) and disease requiring treatment.

iNNOVATE Study; ClinicalTrials.gov ID: NCT02165397.

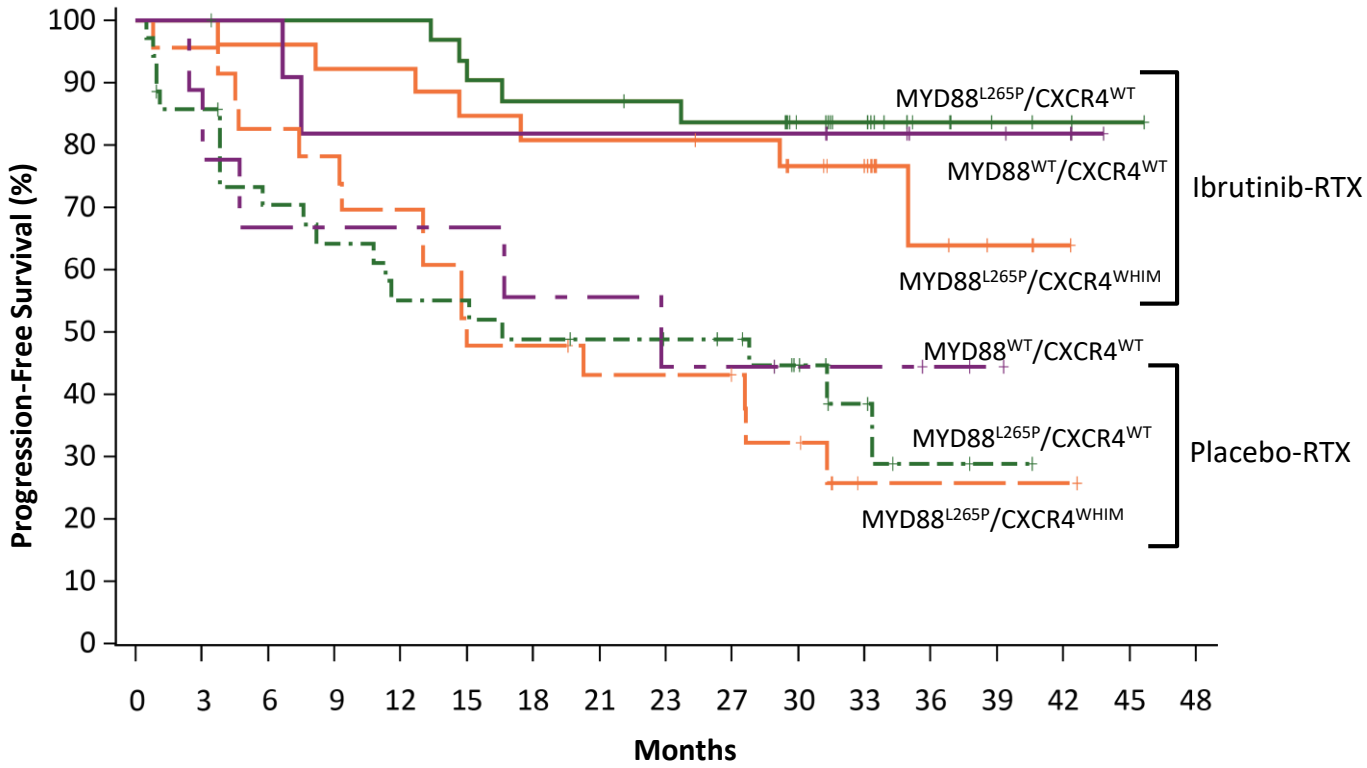
Randomized Study: Progression-Free Survival by Investigator Assessment Prolonged With Ibrutinib-RTX



- **36-month PFS rates: 76% vs 31%**

ASH 2018, iNNOVATE WM; Buske et al.

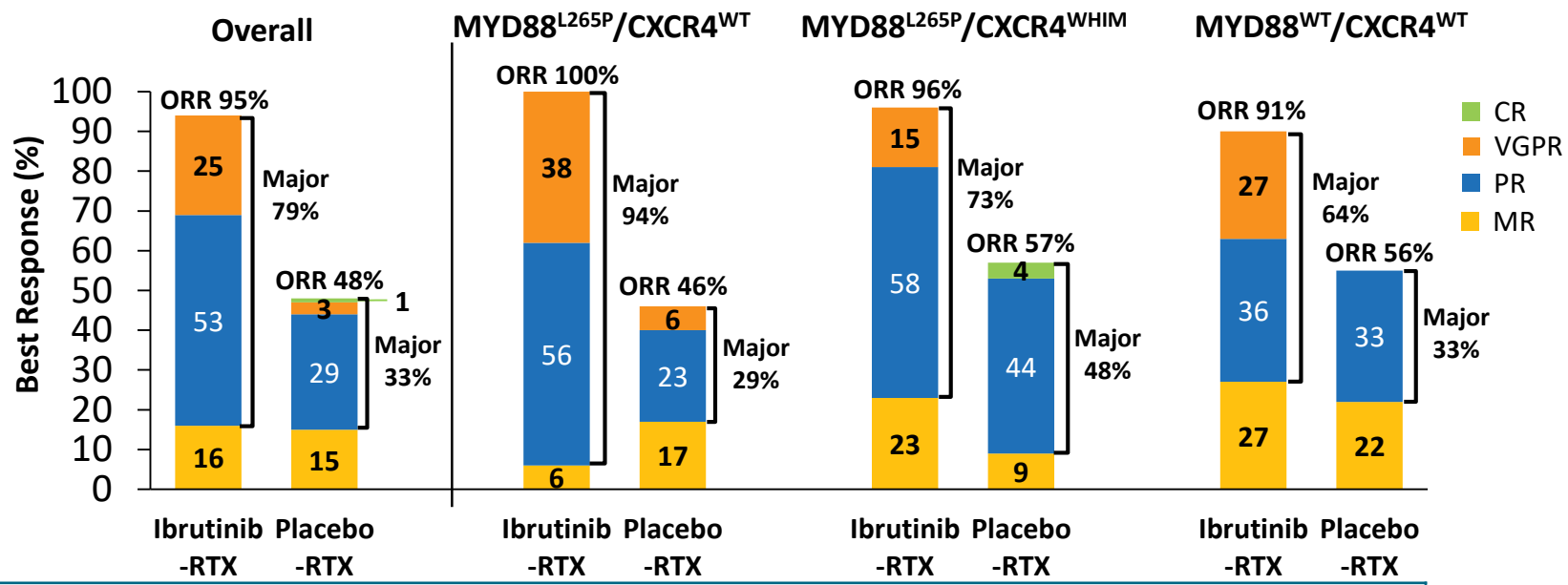
Randomized Study: Progression-Free Survival Benefit With Ibrutinib-RTX Independent of MYD88/CXCR4 Genotype



- **Improved PFS across all genotypes with ibrutinib-RTX**
- **36-month PFS rates**
  - **MYD88^{L265P}/CXCR4^{WT}: 84% vs 29%**
  - **MYD88^{L265P}/CXCR4^{WHIM}: 64% vs 26%**
  - **MYD88^{WT}/CXCR4^{WT}: 82% vs 44%**

ASH 2018, iNNOVATE WM; Buske et al.

Randomized Study: Higher Response Rates[a] With Ibrutinib-RTX Independent of MYD88/CXCR4 Genotype



	Ibrutinib -RTX	Placebo -RTX	Ibrutinib -RTX	Placebo -RTX	Ibrutinib -RTX	Placebo -RTX	Ibrutinib -RTX	Placebo -RTX
Median time to ≥PR, months (range)	2 (1–28)	6 (2–26)	2 (1–28)	5 (2–17)	3 (1–19)	11 (4–18)	6 (1–17)	6 (5–26)
Median time to ≥MR, months (range)	1 (1–18)	3 (1–24)	1 (1–18)	3 (1–24)	1 (1–11)	3 (1–8)	2 (1-17)	3 (2–17)

CR, complete response; MR, minor response; PR, partial response; VGPR, very good partial response.
[a]Following modified 6th IWWM Response Criteria (NCCN 2014); required two consecutive assessments.

Treatment of WM

What comes next?

Improving Ibrutinib (Ibrutinib as a backbone)!

→ ***Rituximab/Ibrutinib – Yes, iNNOVATE***
→ ***Ibrutinib/Proteasome inhibitor?***

European Consortium for Waldenström's Macroglobulinemia
ECWM - Trials 2018/19

Trials First Line

ECWM-1 (Phase III)
DRC versus Bortezomib-DRC
European, over 60 centers

ECWM-2 (Phase II)
Bortezomib-Rituximab/Ibrutinib
European
30 centers

CZAR-1 (ECWM-3 (Phase III)
Carfilzomib/Ibrutinib vs Ibrutinib
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ECWM-R2 Phase II;
Hovon, Greece
Ixazomib/Rituximab/Dex

ECWM-R3
Phase II; France
Idelalisib/GA101

http://www.ecwm.eu/clinical_trials/__Clinical-Trials.html

ECWM-2 - Quartal III 2018

first line WM – single arm phase II

Key eligibility criteria

- Confirmed WM (N=53)
- Measurable disease
  (serum IgM > 0.5 g/dL)
- In need of treatment
- ECOG PS status of 0–2
- Genotyped for MYD88/CXCR4

Treatment

Induction

- Bortezomib SC 1.6/m^2 d1,8,15 cycle 1-6
- Rituximab 375 mg/m2 IV cycle 1, 1400 SC cycle 1-6
- Ibrutinib 420 mg PO continuously

Maintenance

- Rituximab 1400 SC every 2nd month x 12
- Ibrutinib 420 mg PO continously

Study Flow – CZAR-1

Key eligibility criteria

- Confirmed WM (N=184)
- Treatment naïve or relapsed/refractory
- In need of treatment
- No prior treatment with BTK inhibitors or Carfilzomib

1:1 Randomization

Stratification

- MYD88/CXCR4 mutations
- Number of prior regimens (0 vs ≥1)

Arm A
Carfilzomib/Ibrutinib
Oral ibrutinib 420 mg once daily until PD
Carfilzomib 20 mg/m^2 IV d1 cycle 1,
70mg/m^2 IV d 8,15 cycle 1,
70mg/m^2 IV d 1, 8,15 cycle 2-12,
70mg/m^2 IV d 1,15 cycle 13-24

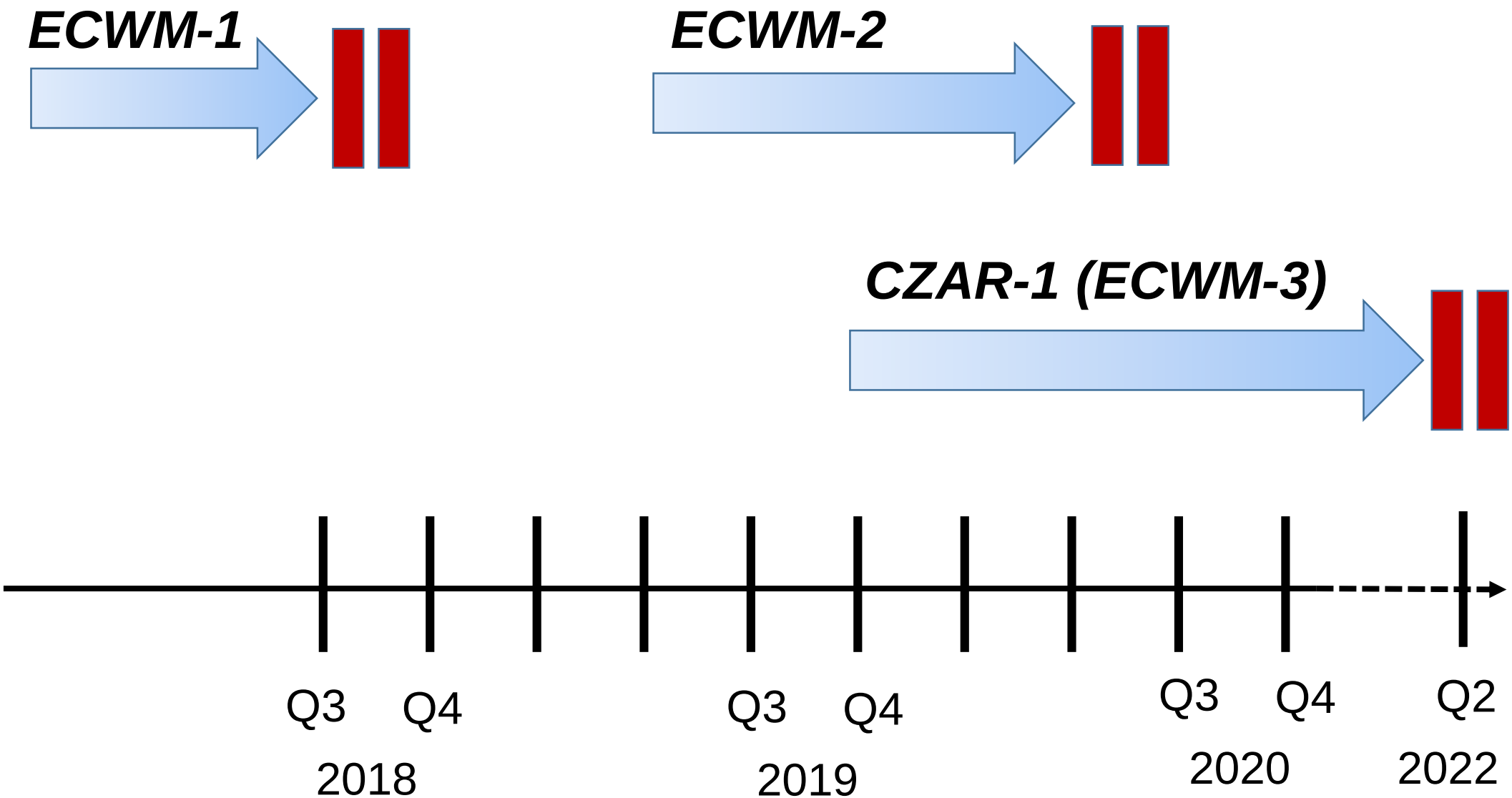
PD
Follow-up for survival

Arm B
Ibrutinib
Oral ibrutinib 420 mg once daily until PD

PD
Follow-up for survival

- **Primary Endpoint:** Rate of CR/VGPR 12 months after start of treatment

ECWM Program



Indolente B - NHL

1. Follikuläres Lymphom (fortgeschrittene Lymphome)
2. Morbus Waldenström
3. Marginalzonenlymphom

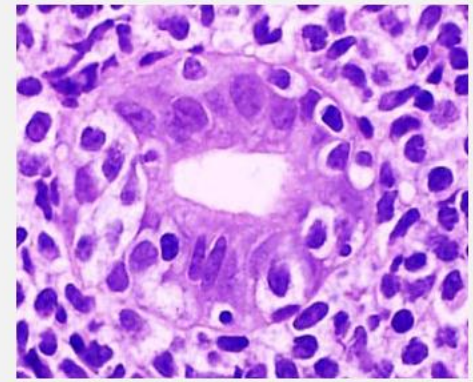
Marginal Zone Lymphoma

Many challenges!

- *Heterogenous disease*
- *No standard treatment*
- *Chemotherapy or chemofree?*

→ *Few prospective registry data!*
→ *Few prospective trials!*

DEUTSCHES MARGINALZONEN-LYMPHOM-REGISTER



Universitätsklinik Ulm * Comprehensive Cancer Center * Albert-Einstein-Allee 11 * 89081 Ulm

Marginalzonen-Lymphom-Register
Comprehensive Cancer Center
Universitätsklinik Ulm
Albert-Einstein-Allee 11
89081 Ulm

Studienzentrale

Tel. 0731 - 500 65801
0731 - 500 65888

Telefax. 0731 - 500 65822

E-mail: mzol.register@uniklinik-ulm.de

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

Abbildung 1: Aktivierte Zentren (Stand April 2017)

Diese illustrative Abbildung wurde urheberrechtlichen Gründen entfernt.

Aktivierte Zentren (n = 91)

Seit Mai 2015

- 435 Patienten 2/2019
- 202 Patienten validiert

2. Förderperiode genehmigt

Inklusive Biosampling Program (In Kooperation mit C. Pott/M. Kneba)

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

Marginal Zone Lymphoma

Many challenges!

- *Heterogenous disease*
- *No standard treatment*
- *Chemotherapy or chemofree?*

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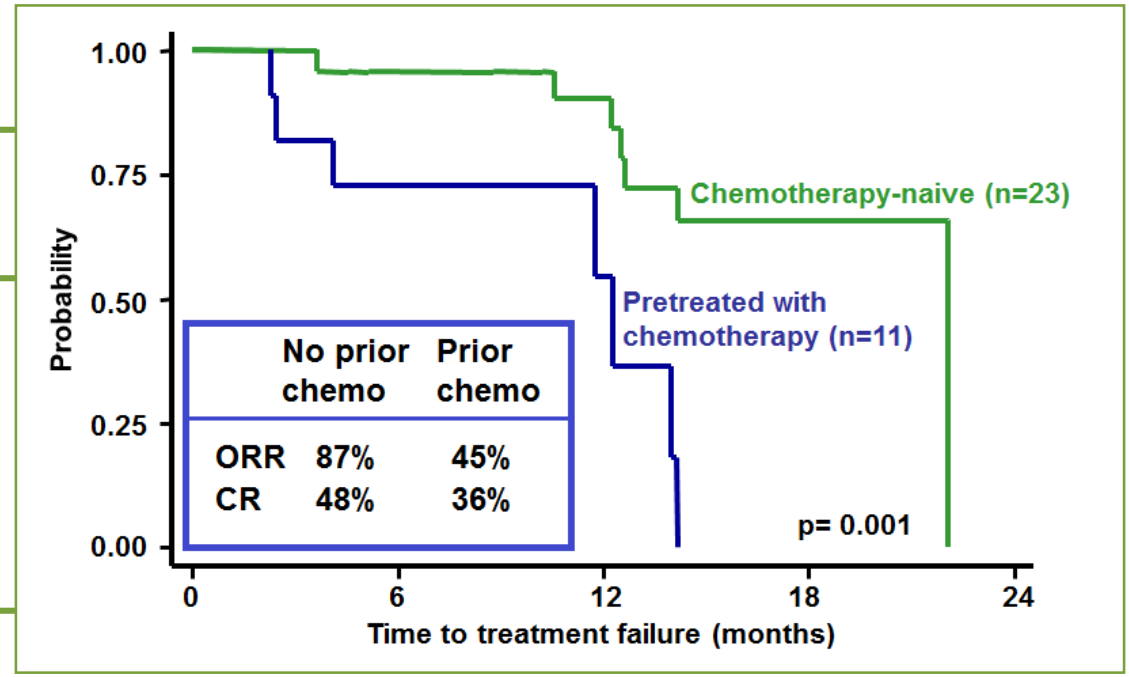
Indolente Lymphome

Unser Ziel: „chemofreie" Ansätze

Rituximab activity in MALT lymphoma

response	*n*	*%*
ORR	**25**	**73**
SD	**6**	**18**
PD	**3**	**9**



34 pts, 11 with prior chemotherapy,
15 gastric, 20 stage IV

IELSG phase II study, Conconi et al. Blood 2003

OLYMP-1

OBINUTUZUMAB in MARGINAL ZONE LYMPHOMA

Key eligibility criteria

- Treatment naïve confirmed MZoL (N=56)
  - -- nodal/extranodal/splenic
- In need of treatment
- Not eligible or refractory to local therapy

Treatment

Induction:

Cycle 1 (28 days cycle): Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1,8,15

Cycle 2-6 (28 days cycle): Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1

Maintenance

Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1 every 8 weeks for a maximum of 12 infusions

First line MZoL – single arm phase II German Study

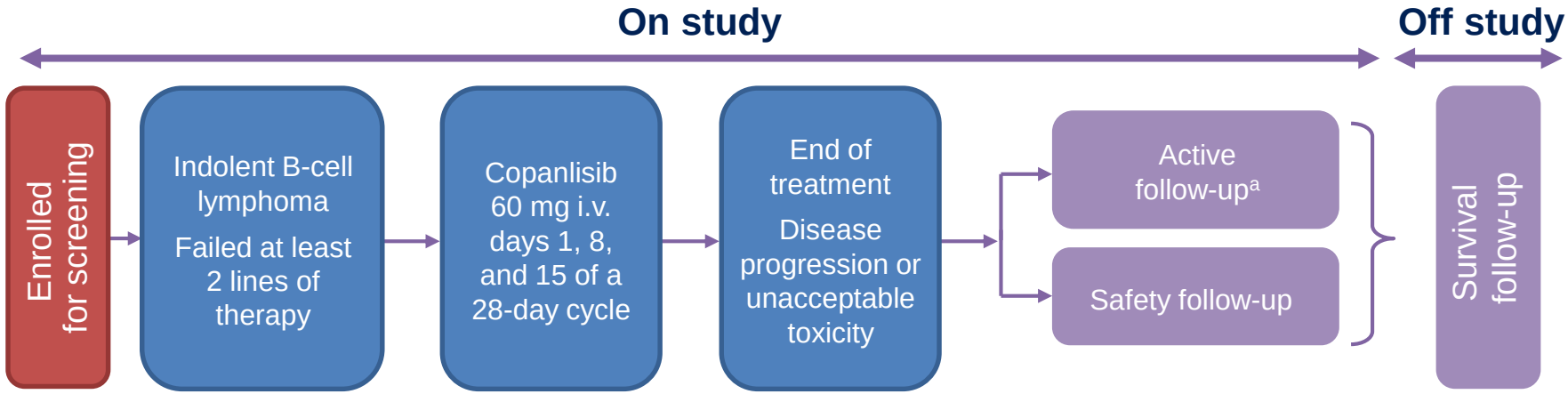
Copanlisib in patients with relapsed or refractory indolent B-cell lymphoma: primary results of the pivotal CHRONOS-1 study

Martin Dreyling,[1] Armando Santoro,[2] Luigina Mollica,[3] Sirpa Leppä,[4] George A Follows,[5] Georg Lenz,[6] Won Seog Kim,[7] Arnon Nagler,[8] Panayiotis Panayiotidis,[9] Judit Demeter,[10] Muhit Özcan,[11] Marina Kosinova,[12] Krimo Bouabdallah,[13] Franck Morschhauser,[14] Don A Stevens,[15] David Trevarthen,[16] Marius Giurescu,[17] Lisa Cupit,[18] Li Liu,[18] Karl Köchert,[17] Henrik Seidel,[17] Carol Peña,[18] Shuxin Yin,[18] Florian Hiemeyer,[17] Jose Garcia-Vargas,[18] Barrett H Childs,[18] Pier Luigi Zinzani[19]

[1]Medizinische Klinik und Poliklinik III, Klinikum der Universität München-Grosshadern, Munich, Germany; [2]Department of Oncology and Hematology, Humanitas Cancer Center, Humanitas Clinical and Research Center, Rozzano, Italy; [3]Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada; [4]Helsinki University Central Hospital Cancer Center, Helsinki, Finland; [5]Department of Haematology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [6]Translational Oncology, University Hospital Münster, Münster, Germany; [7]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, South Korea; [8]Chaim Sheba Medical Center, Tel Aviv University, Tel-Hashomer, Israel; [9]Laikon University Hospital, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [10]First Department of Internal Medicine, Division of Haematology Semmelweis University, Budapest, Hungary; [11]Department of Hematology, Ankara University School of Medicine, Ankara, Turkey; [12]Kemerovo Regional Clinical Hospital, Kemerovo, Russian Federation; [13]Service d'Hématologie et de Thérapie Cellulaire, University Hospital of Bordeaux, Pessac, France; [14]CHRU - Hôpital Claude Huriez, Lille, France; [15]Norton Cancer Institute, Louisville, KY, USA; [16]Comprehensive Cancer Care and Research Institute of Colorado, Englewood, CO, USA; [17]Pharmaceutical Division, Bayer AG, Berlin, Germany; [18]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; [19]Institute of Hematology "L. e A. Seràgnoli", University of Bologna, Bologna, Italy

14th International Conference on Malignant Lymphoma, June 14-15, 2017, Lugano, Switzerland

Study design



Lymphoma types

- FL (grades 1-3a)
- MZL
- SLL
- LPL / WM

Primary endpoint

- ORR[1] by central review

Secondary endpoints

- PFS
- DoR
- OS
- Safety
- Quality of life

Tertiary endpoints

- Disease control rate
- Duration of stable disease
- ECOG scale
- Lesion size
- EQ-5D questionnaire, visual analog scale

- [a]Patients who discontinued treatment for any reason other than progressive disease entered active follow-up

DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EQ-5D, EuroQoL five dimensions questionnaire; ORR objective response rate; OS, overall survival; PFS, progression-free survival

- 1. Cheson et al. *J Clin Oncol* 2007; 25: 579-586

Primary endpoint: ORR

	FL (*n*=104)	MZL (*n*=23)	SLL (*n*=8)	LPL / WM (*n*=6)	Total (*N*=142)[a]
Best response, *n* (%)					
Complete response	15 (14.4%)	2 (8.7%)	0	0	17 (12.0%)
Partial response	46 (44.2%)	14 (60.9%)	6 (75.0%)	1 (16.7%)	67 (47.2%)
Stable disease	35 (33.7%)	4 (17.4%)	1 (12.5%)	3 (50.0%)	42 (29.6%)
Progressive disease	2 (1.9%)	0	1 (12.5%)	0	3 (2.1%)
NE / NA	6 (5.8%)	3 (13.0%)	0	2 (33.3%)	12 (8.5%)
ORR, *n* (%)	61 (58.7%)	16 (69.6%)	6 (75.0%)	1 (16.7%)	84 (59.2%)
95% CI	48.6-68.2	47.1-86.8	34.9-96.8	0.4-64.1	50.6-67.3
Disease control rate, *n* (%)	91 (87.5%)	20 (87.0%)	7 (87.5%)	4 (66.7%)	122 (85.9%)
95% CI	79.6-93.2	66.4-97.2	47.4-99.7	2.3-95.7	79.1-91.2

- In patients who were refractory to the last regimen, the ORR was 60.5% (95% CI 49.3-70.9)

[a]Full analysis set; includes all treated patients
CI, confidence interval; NA, not available; NE, not evaluable

COUP-1

Copanlisib and Rituximab in Marginalzone Lymphoma

Key eligibility criteria

- Treatment naïve and relapsed confirmed MZoL (N=56)
  - -- nodal/extranodal/splenic
- In need of treatment
- Not eligible or refractory to local therapy

Treatment

Induction (Cycle 1-6, 28 days cycle):

Copanlisib: 60 mg/kg days 1, 8, 15

Rituximab: 375 mg/m^2 day 1

Maintenance

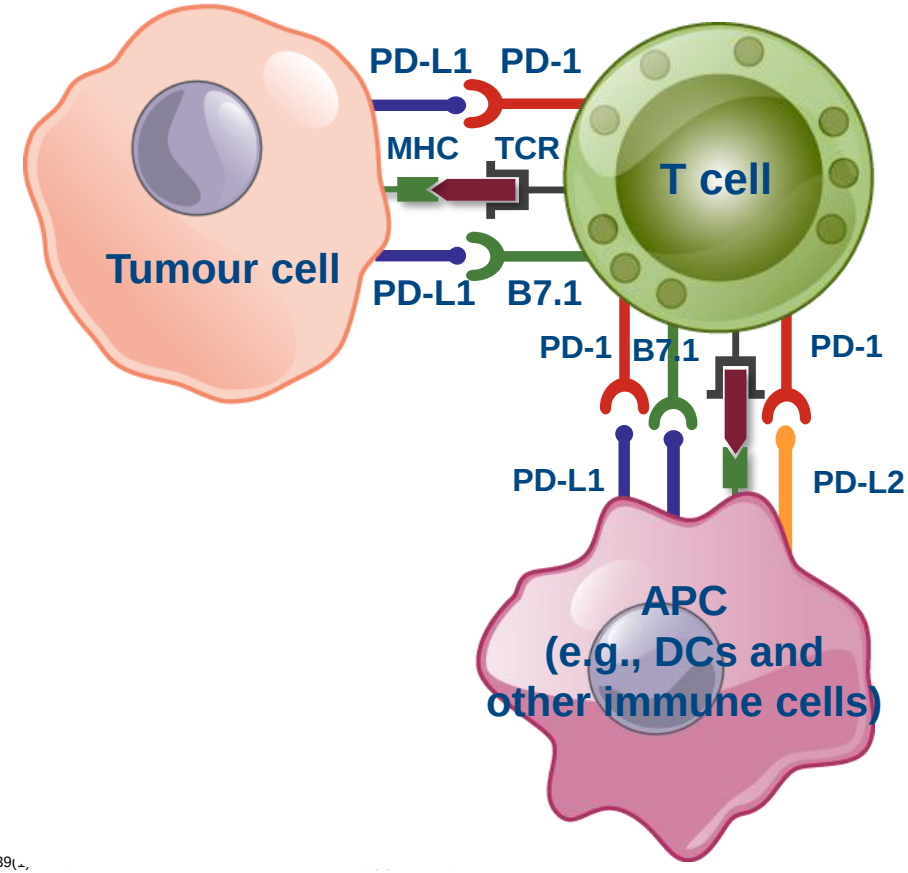
Copanlisib: 60 mg/kg i.v. fixed dose day 1 and day 8 every 8 weeks x 12

Rituximab: 375 mg/m^2 day 1 every 8 weeks x 12

First line MZoL – single arm phase II German/Austrian Study

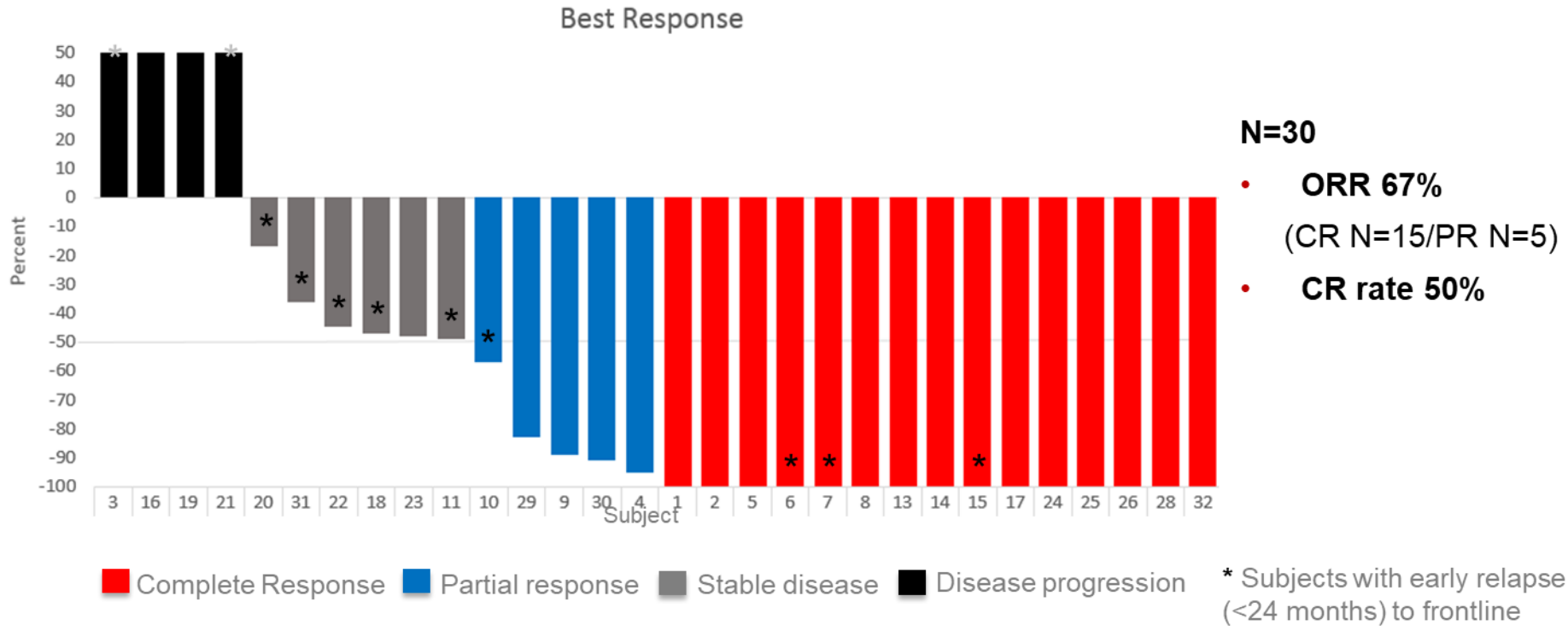
INHIBITING ANTI-TUMOUR T-CELL ACTIVITY
The PD-L1/PD-1 Pathway

- Stimulatory and inhibitory factors are involved at every step of the cancer-immunity cycle[1]
- Immune checkpoint molecule PD-L1 negatively regulates T-cell function[1,2]
  - Tumour cells and tumour-infiltrating immune cells express PD-L1[3,4]
- PD-L1 can inhibit anti-tumour T-cell response and block T-cell–mediated tumour killing by binding to its receptors, PD-1 and B7.1 (CD80)[1-4]
- Inhibiting the interaction between PD-L1 and PD-1 and B7.1 reinvigorates and enhances anti-cancer immunity[3-5]
  - Preserving the PD-L2/PD-1 interaction may preserve immune homeostasis in normal tissues[5-7]



References: 1. Chen DS, Mellman I. *Immunity.* 2013;39(1);
3. Herbst R, et al. *Nature.* 2014;515(7528):563-567; 4. Powles T, et al. *Nature*. 2014;515(7528):558-562; 5. Chen DS, et al. *Clin Cancer Res.* 2012;18(24):6580-6587; 6. Akbari O, et al. *Mucosal Immunol.* 2010;3(12):81-91; 7. Matsumoto K, et al. *Biochem Biophys Res Commun*. 2008;365(1):170-175.

High Complete Response Rates with Pembrolizumab in Combination with Rituximab in Patients with Relapsed Follicular Lymphoma: Results of an Open-label, Phase II Study



Loretta J. Nastoupil et al., ASH 2017

POLE-1

Pembrolizumab in Marginal Zone Lymphoma

Key eligibility criteria

- Treatment naïve and relapsed confirmed MZoL (N=56)
  - -- nodal/extranodal/splenic
- In need of treatment
- Not eligible or refractory to local therapy

Treatment

Cycle 1 (21 days cycle):

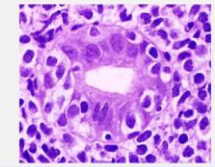
- Pembrolizumab:200 mg IV fixed dose day 2
- Rituximab: 375 mg/m^2 day 1, 8, 15

Cycle 2-18 (21 days cycle) or until progression or non-tolerable toxicity:

- Pembrolizumab: 200 mg IV fixed dose day 1
- Rituximab: 375 mg/m^2 day 1 every second cycle

MZoL – single arm phase II German-Italian Study

Deutsches Marginalzonen-Lymphom-Register



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Marginalzonen-Lymphom-Register
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Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

MZL - Programm

Registry

Clinical Trials

German Lymphoma Alliance

OLYMP-1

OBINUTUZUMAB in MARGINAL ZONE LYMPHOMA

Key eligibility criteria
- Treatment naive confirmed MZoL (N=56)
  -- nodal/extranodal/splenic
- In need of treatment
- Not eligible or refractory to local therapy

Treatment

Induction:
Cycle 1 (28 days cycle): Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1,8,15

Cycle 2-6 (28 days cycle): Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1

Maintenance
Obinutuzumab (GA101) 1000mg i.v. fixed dose day 1 every 8 weeks for a maximum of 12 infusions

First line MZoL – single arm phase II German Study

COUP-1

Copanlisib and Rituximab in Marginalzone Lymphoma

Key eligibility criteria
- Treatment naive and relapsed confirmed MZoL (N=56)
  -- nodal/extranodal/splenic
- In need of treatment
- Not eligible or refractory to local therapy

Treatment

Induction (Cycle 1-6, 28 days cycle):
Copanlisib: 60 mg/kg days 1, 8, 15
Rituximab: 375 mg/m² day 1

Maintenance
Copanlisib: 60 mg/kg i.v. fixed dose day 1 and day 8 every 8 weeks x 12
Rituximab: 375 mg/m² day 1 every 8 weeks x 12

First line MZoL – single arm phase II German/Austrian Study

POLE-1

Pembrolizumab in Marginal Zone Lymphoma

Key eligibility criteria
- Treatment naïve and relapsed confirmed MZoL (N=56)
  -- nodal/extranodal/splenic
- In need of treatment
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Treatment

Cycle 1 (21 days cycle):
- Pembrolizumab:200 mg IV fixed dose day 2
- Rituximab: 375 mg/m² day 1, 8, 15

Cycle 2-18 (21 days cycle) or until progression or non-tolerable toxicity:
- Pembrolizumab: 200 mg IV fixed dose day 1
- Rituximab: 375 mg/m² day 1 every second cycle

MZoL – single arm phase II German-Italian Study

GLA Studientreffen Göttingen November 2018