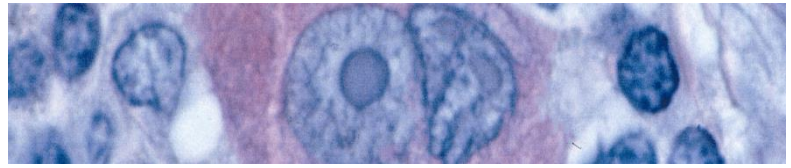
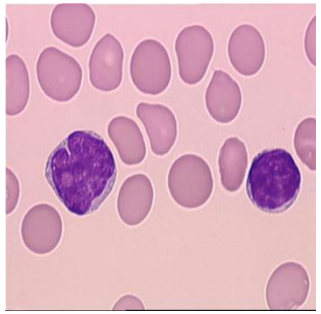
Kompetenznetz Maligne Lymphome



SPEED REPORT:

INDOLENTE LYMPHOME

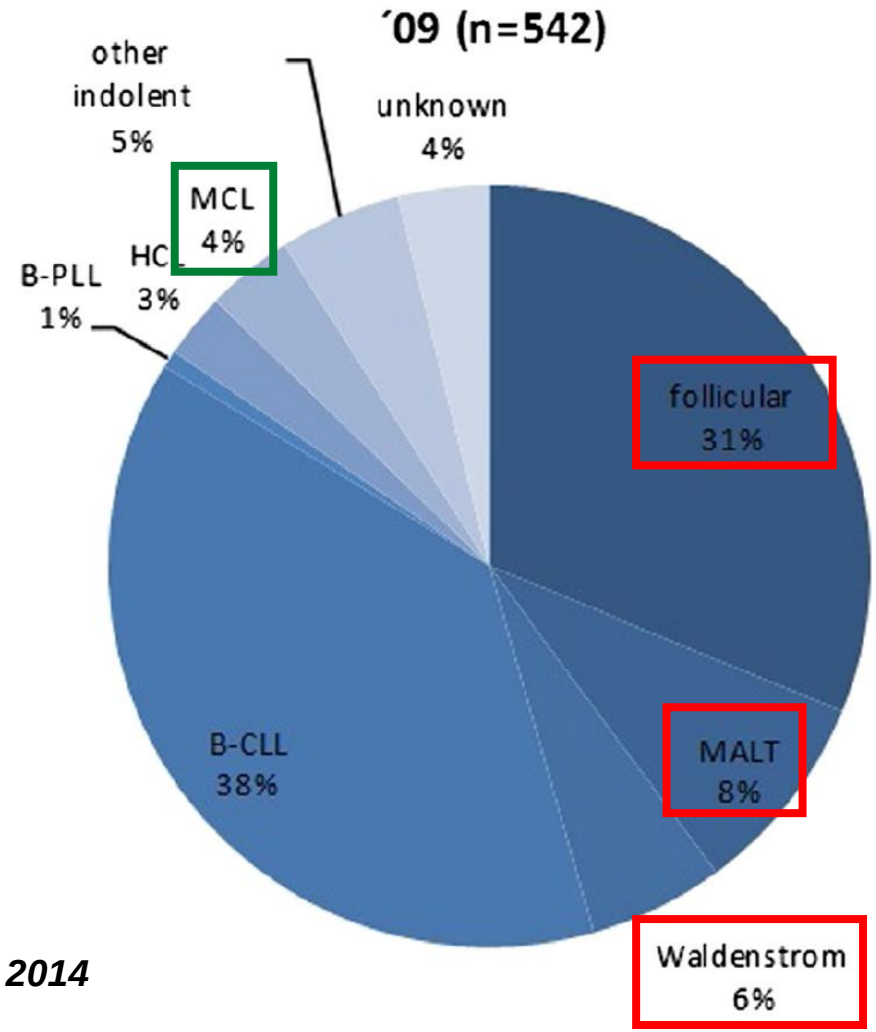


German Lymphoma Alliance

European MCL Network

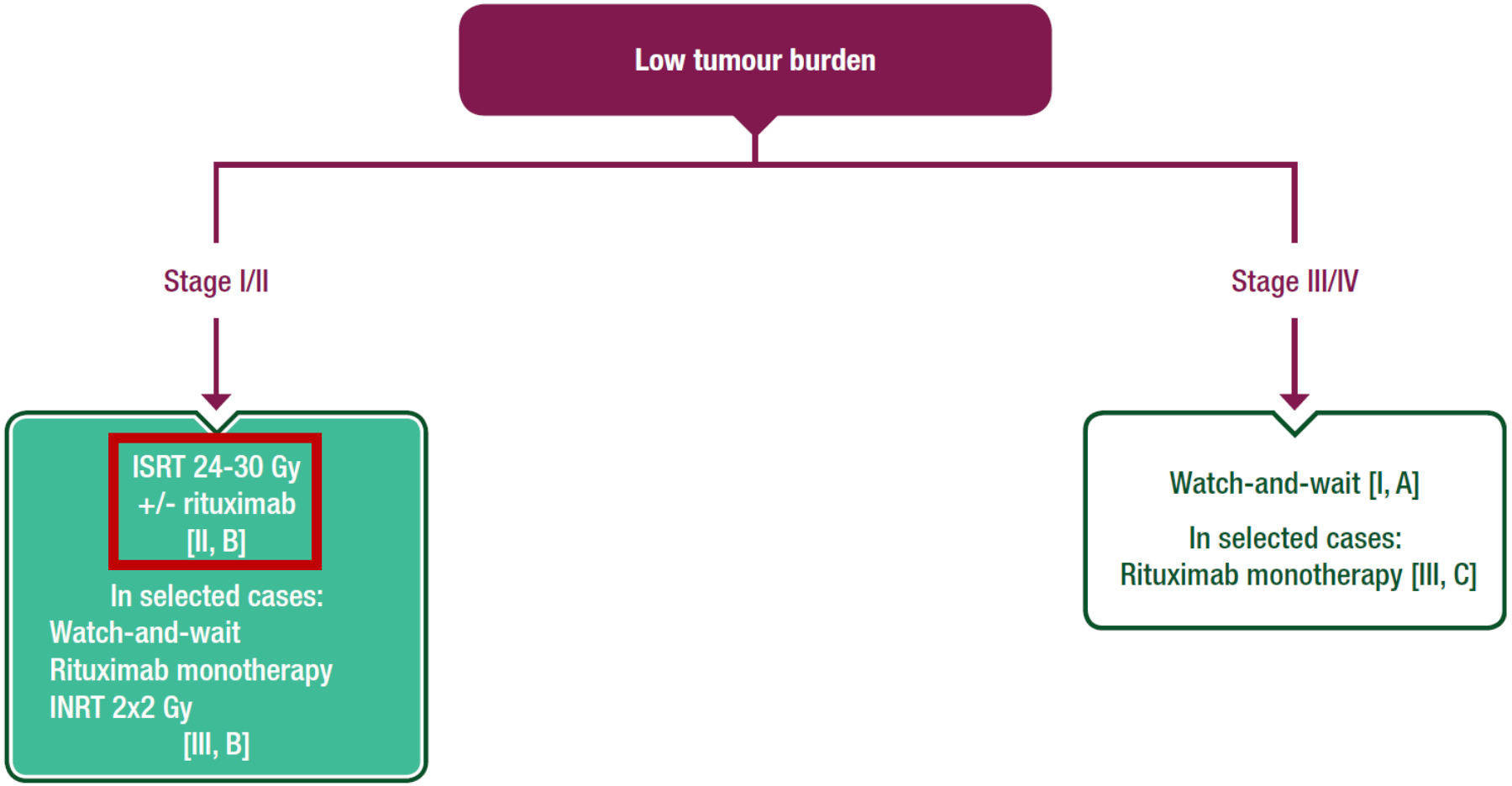
Prof. Dr. Martin Dreyling
Medizinische Klinik III
LMU München

Indolent Lymphoma
Frequency of subtypes



Schmidt, Leuk Lymph 2014

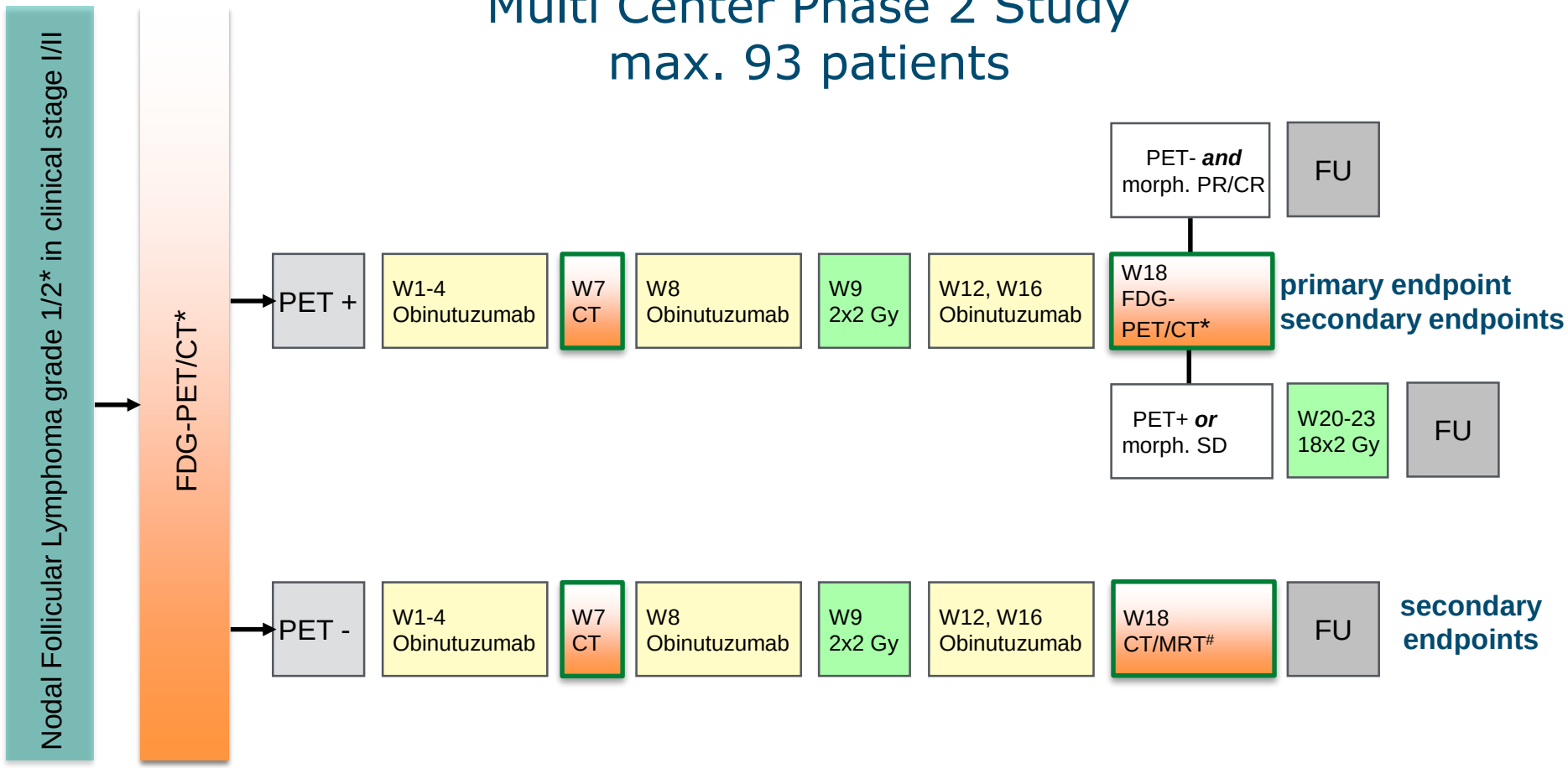
Follicular lymphoma
ESMO/EHA therapeutic algorithm



Dreyling, Ann Oncol 2021

GAZAI

Multi Center Phase 2 Study
max. 93 patients



= only in case of initially enlarged PET negative lymph nodes

* = centrally reviewed

König et al, Trials, 2019

FORT*plus*

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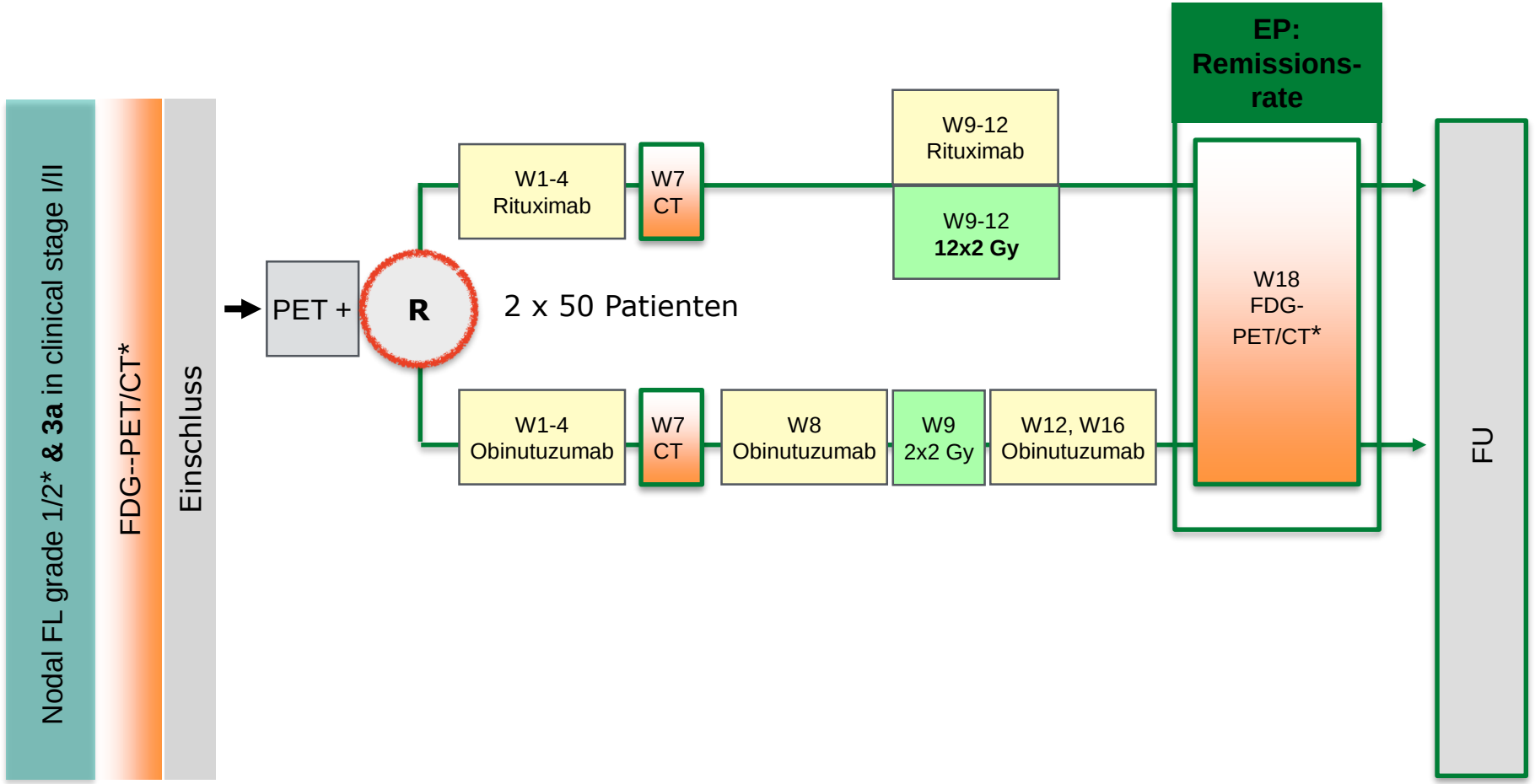
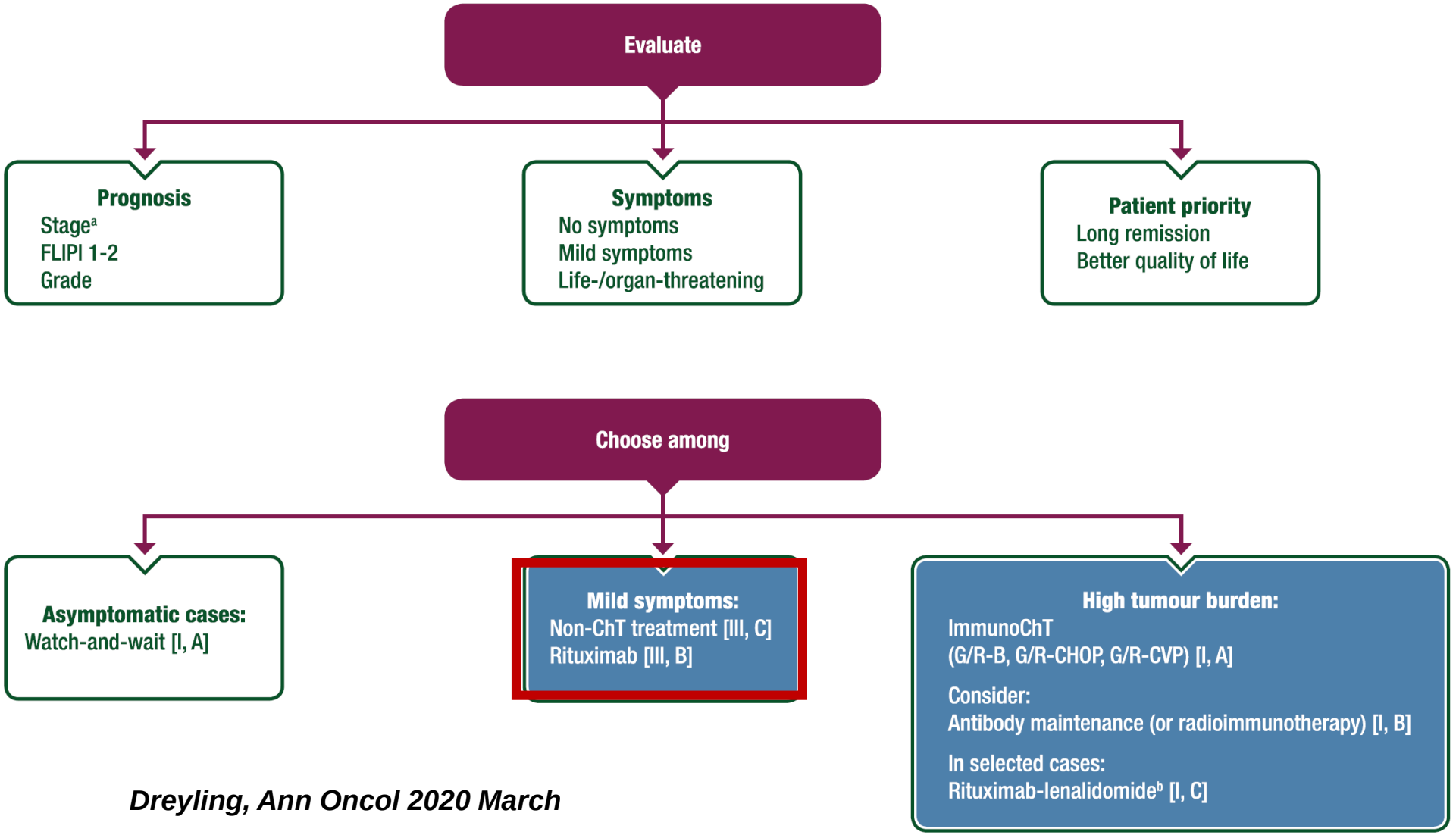
Non-inferiority design



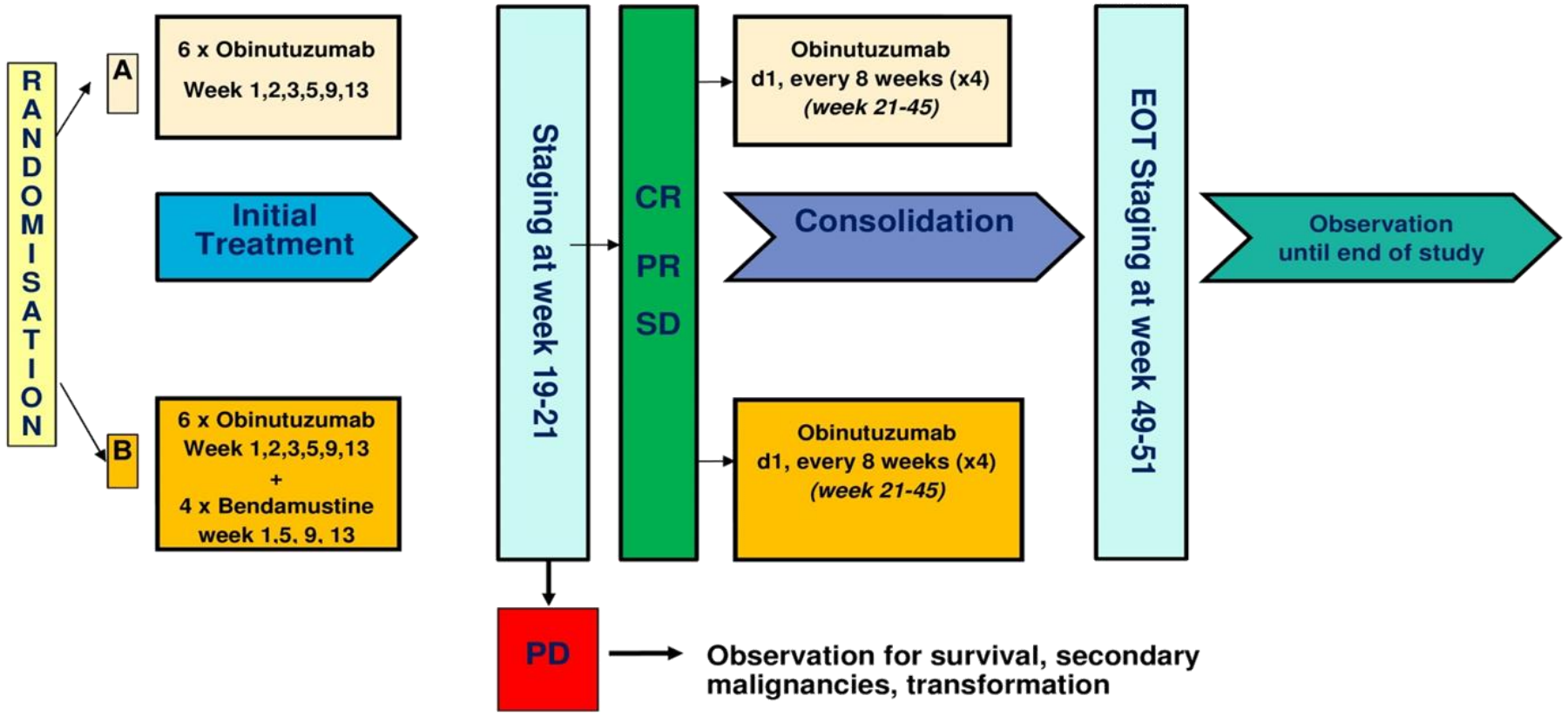
* = centrally reviewed

Follicular lymphoma
ESMO/EHA therapeutic algorithm

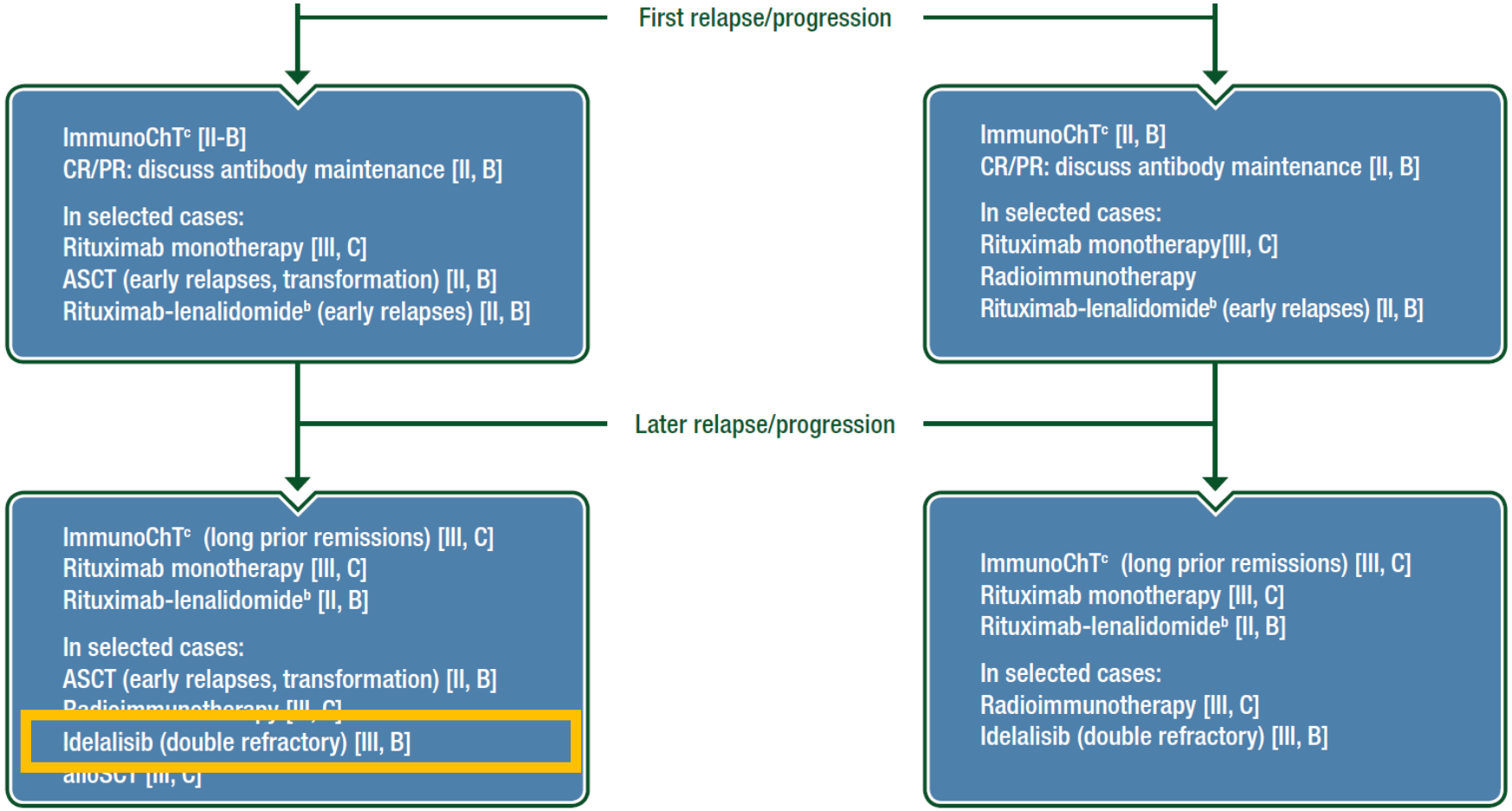


Dreyling, Ann Oncol 2020 March

CHEMOTHERAPY VS TARGETED THERAPY:
GABE STUDIE



Follicular lymphoma
ESMO/EHA therapeutic algorithm



Dreyling, Ann Oncol 2021 March

Relapsed Follicular lymphoma
R +/- novel drug

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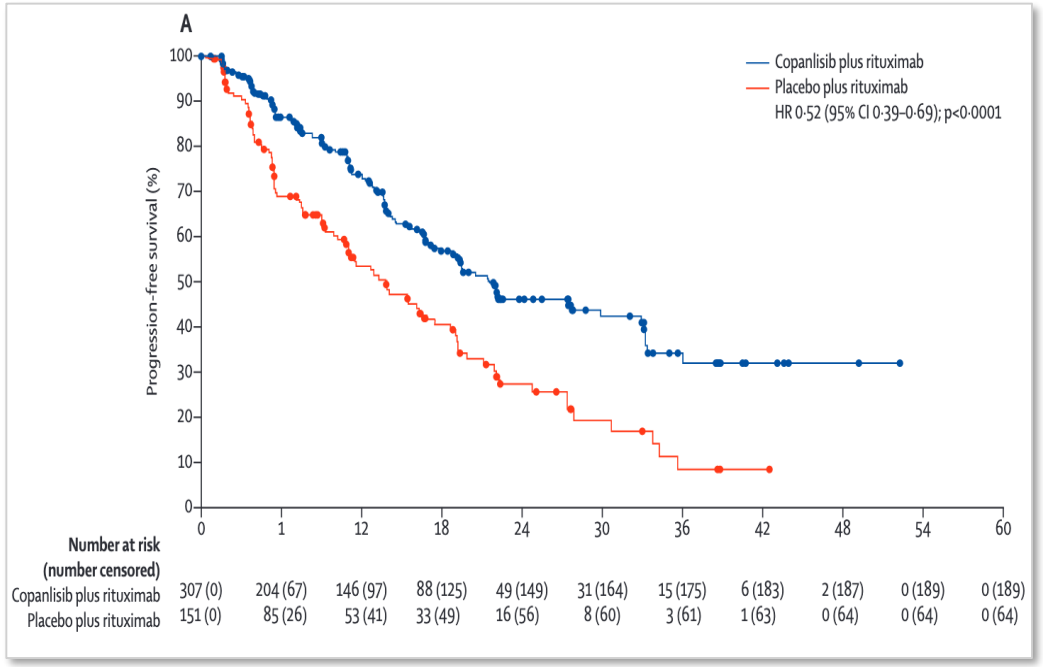
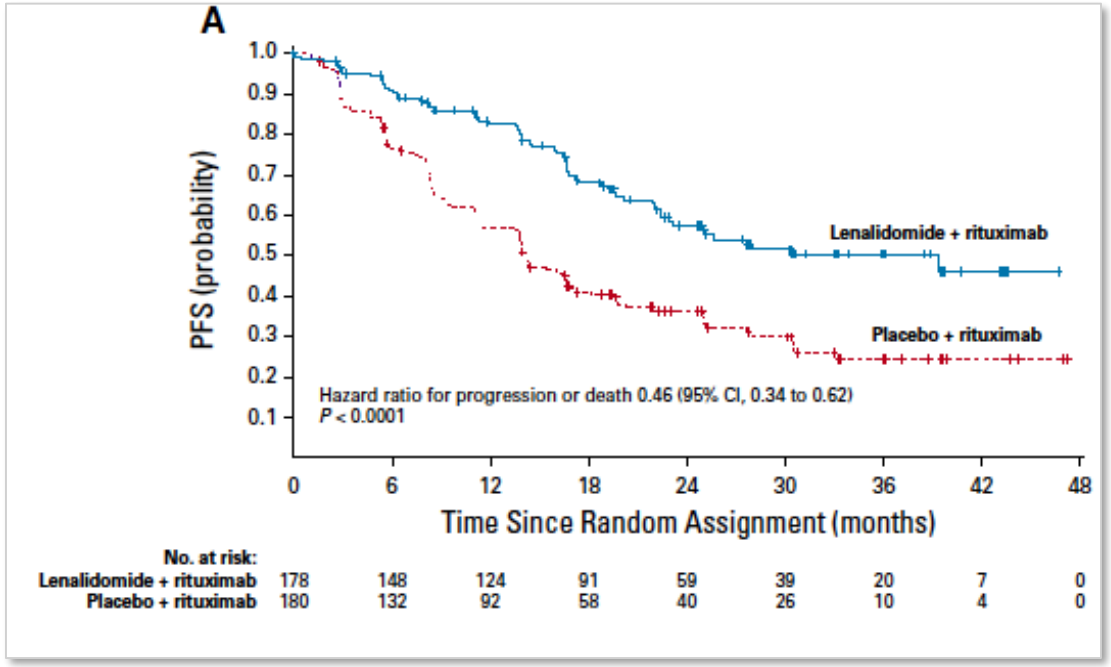
Copanlisib plus R



OR 81%, CR 34%
Median PFS 21,5 vs. 13.8 months
HR 0,52 [95% CI 0·39–0·69]; p<0·0001

Matasar Lancet Oncol 2021

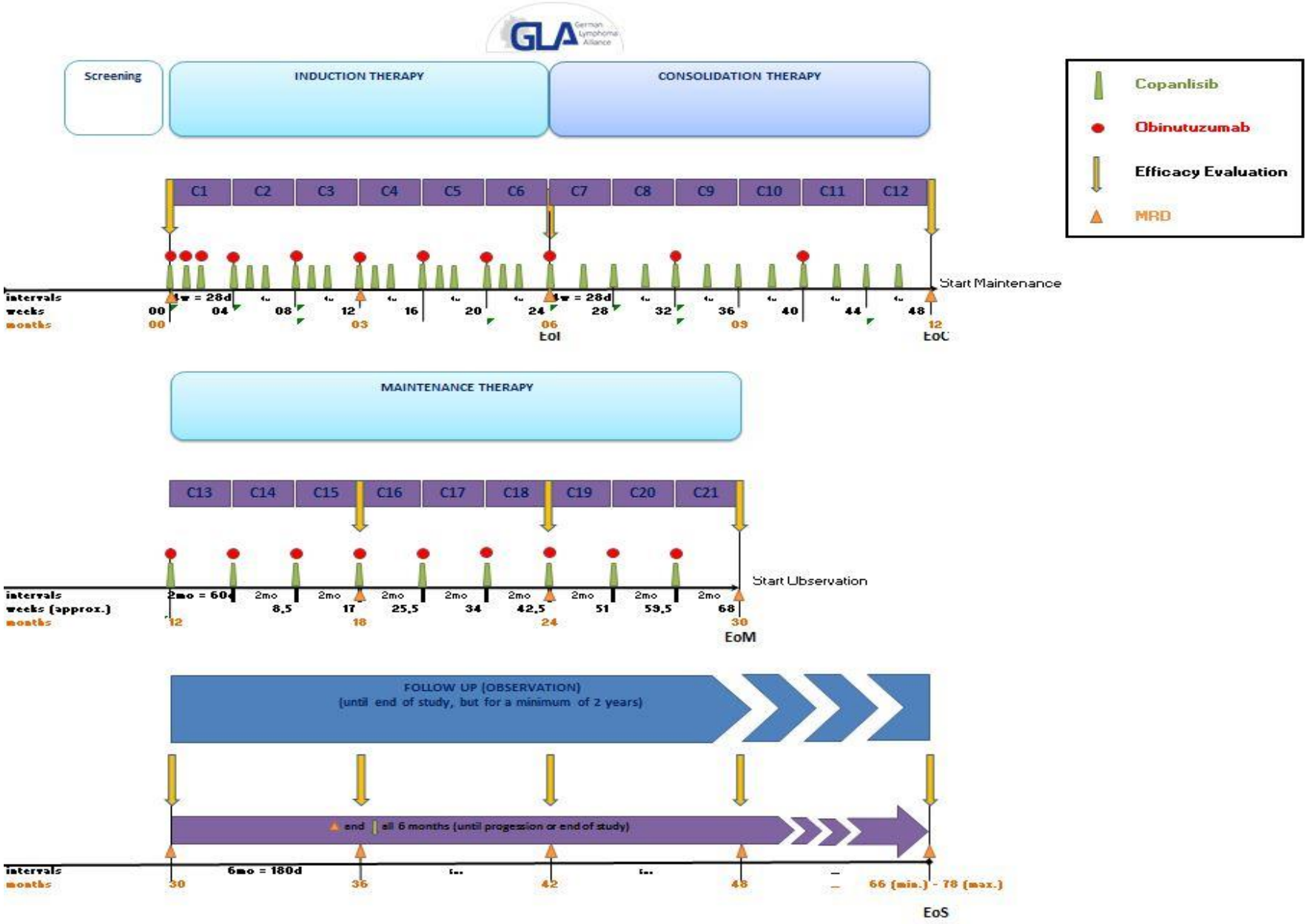
Lenalidomid plus R



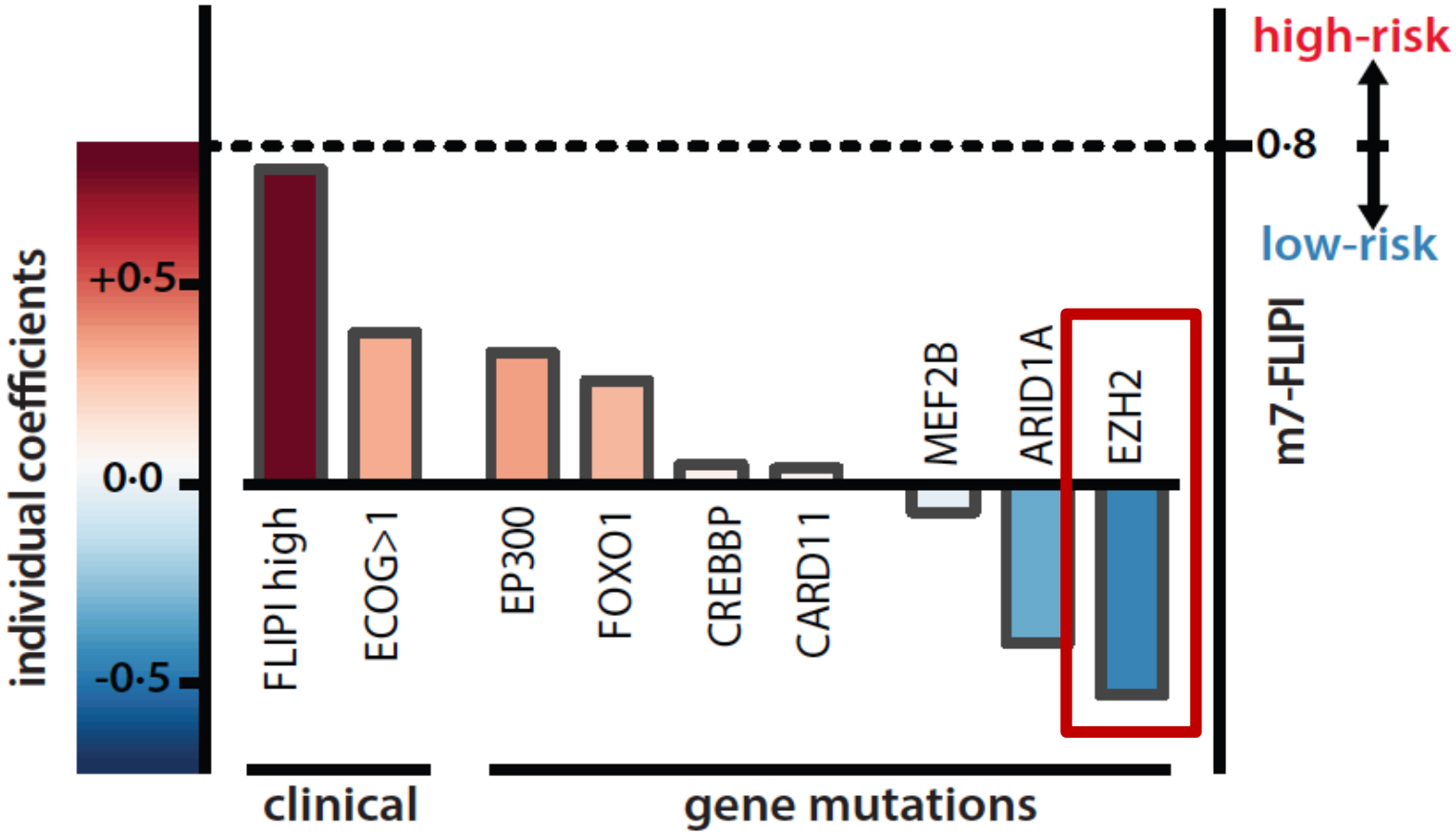
OR 78%, CR 34%.
Median PFS 39 vs. 14 months
HR 0.46 (95% CI, 0.34 to 0.62; p= 0.001)

Leonhard JCO 2019

ALTERNATIVE-C Flowchart



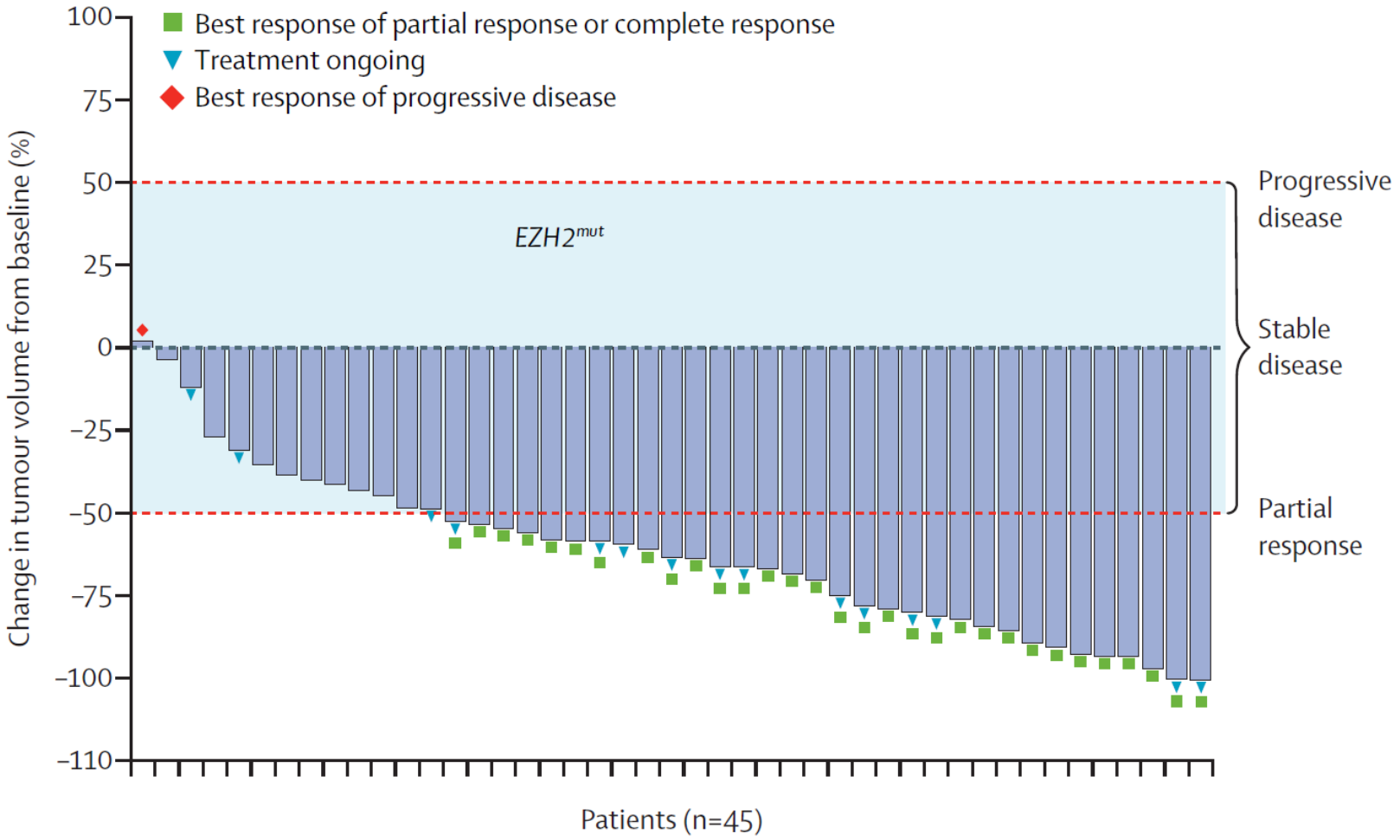
Follicular lymphoma
clinicogenetic risk algorithm



Pastore, Lancet Oncology 2015

Relapsed Follicular lymphoma

EZH2-inhibitor: Response rates



MORSCHHAUSER, LANCET ONCOL 2020

Relapsed Follicular lymphoma
Bispecific antibody (n=62)

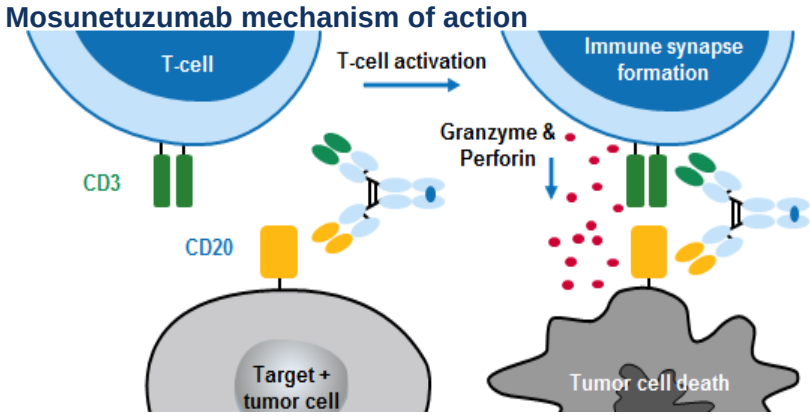
Follicular lymphoma (FL) remains an incurable disease despite available therapies

Patients with FL having received ≥2 prior systemic therapies typically have a poor prognosis[1]

High-risk subgroups include patients who:

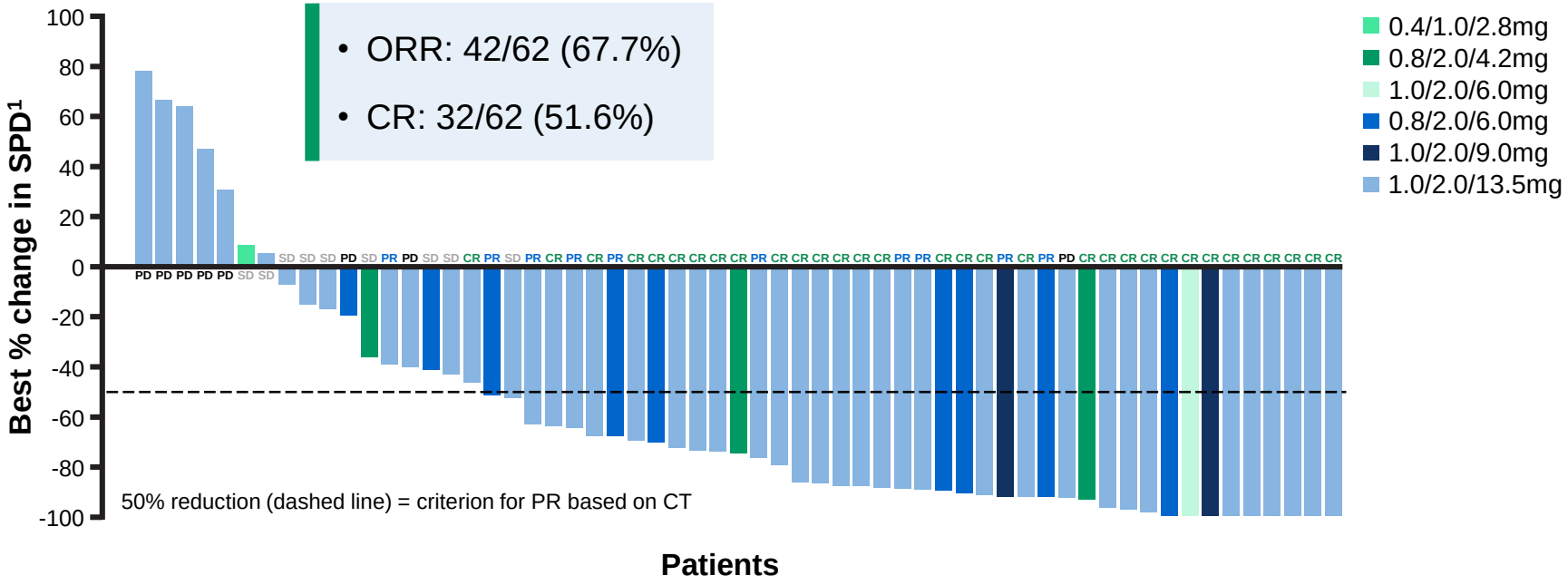
- **Have progression of disease within 24 months of frontline treatment (POD24)[2]**
- **Are refractory to both a prior anti-CD20 antibody and an alkylating agent (double refractory)**

Mosunetuzumab is a full-length, fully humanized immunoglobulin G1 CD20xCD3 bispecific antibody that redirects T cells to engage and eliminate malignant B cells



ASSOULINE, ASH2020: #702

Relapsed Follicular lymphoma
Bispecific antibody (n=62)



ASSOULINE, ASH2020: #702

Relapsed follicular lymphoma
Therapy: Role of CAR T-cells ?

Follicular lymphoma
GLA Studien 2021

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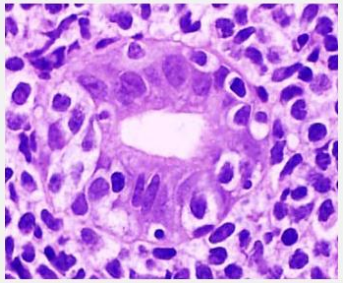
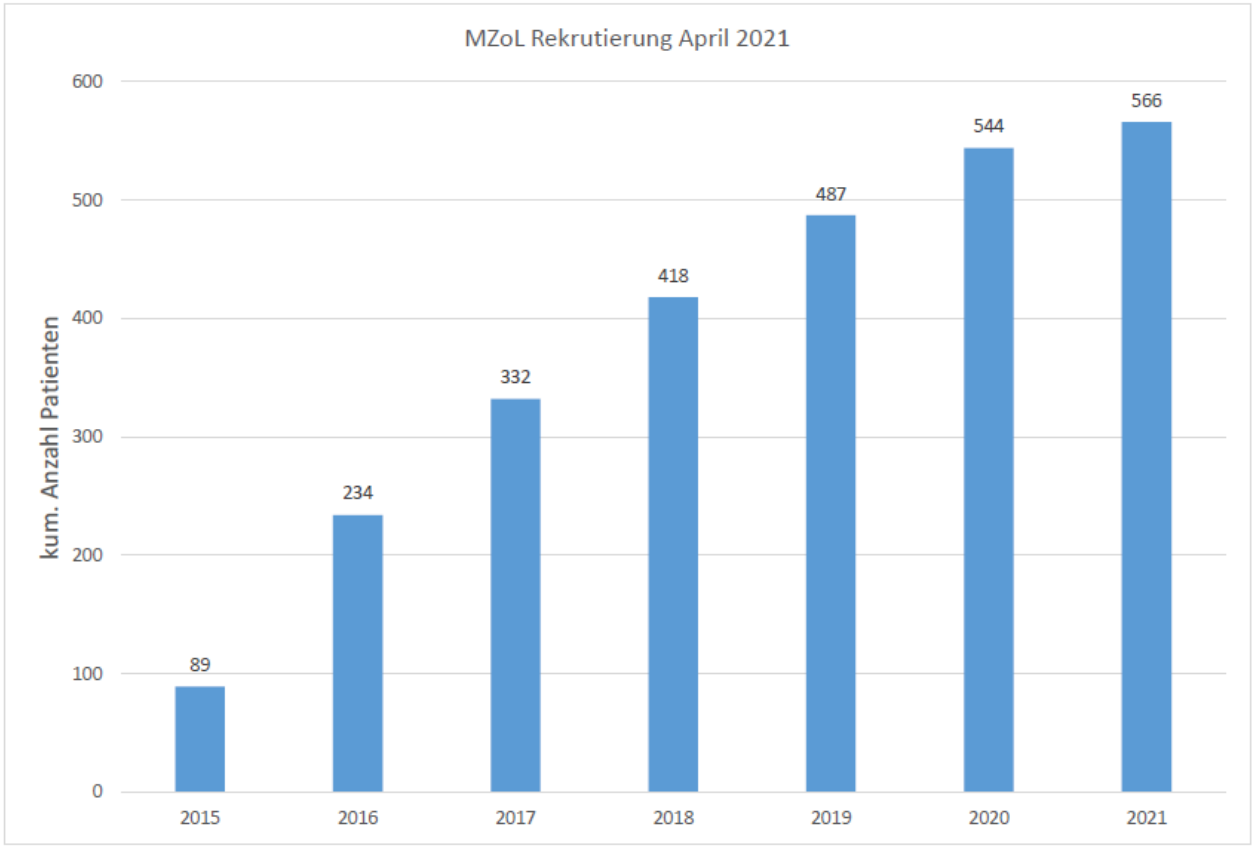
Alternative 1:	*Alternative 2:*	*medically non-fit:*
G-Ibru	G-Copanlisib	G +/- Bendamustine
↓	↓	↓
G-Ibru maintenance	G-Copanlisib maintenance	G maintenance

Relapse

R2 +/- Tazemetostat	R2 +/- Tafasitamab	R2 vs Mosunetuzumab-R

Deutsches Marginalzonen-Lymphom-Register





Biosampling begonnen.

56 Patienten fortlaufend

(Wangenabstrich, DNA/RNA, cfDNA)

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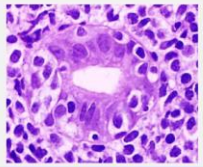
DEUTSCHES MARGINALZONEN-LYMPHOM-REGISTER



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

Marginalzonen-Lymphom-Register
Comprehensive Cancer Center
Universitätsklinik Ulm
Albert-Einstein-Allee 11
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0731 - 500 65888
Telefax. 0731 - 500 65822
E-mail: mzol.register@uniklinik-ulm.de

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

MZL - Programm

Registry

Clinical Trials

German Lymphoma Alliance

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

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/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
- Not eligible or refractory to local therapy

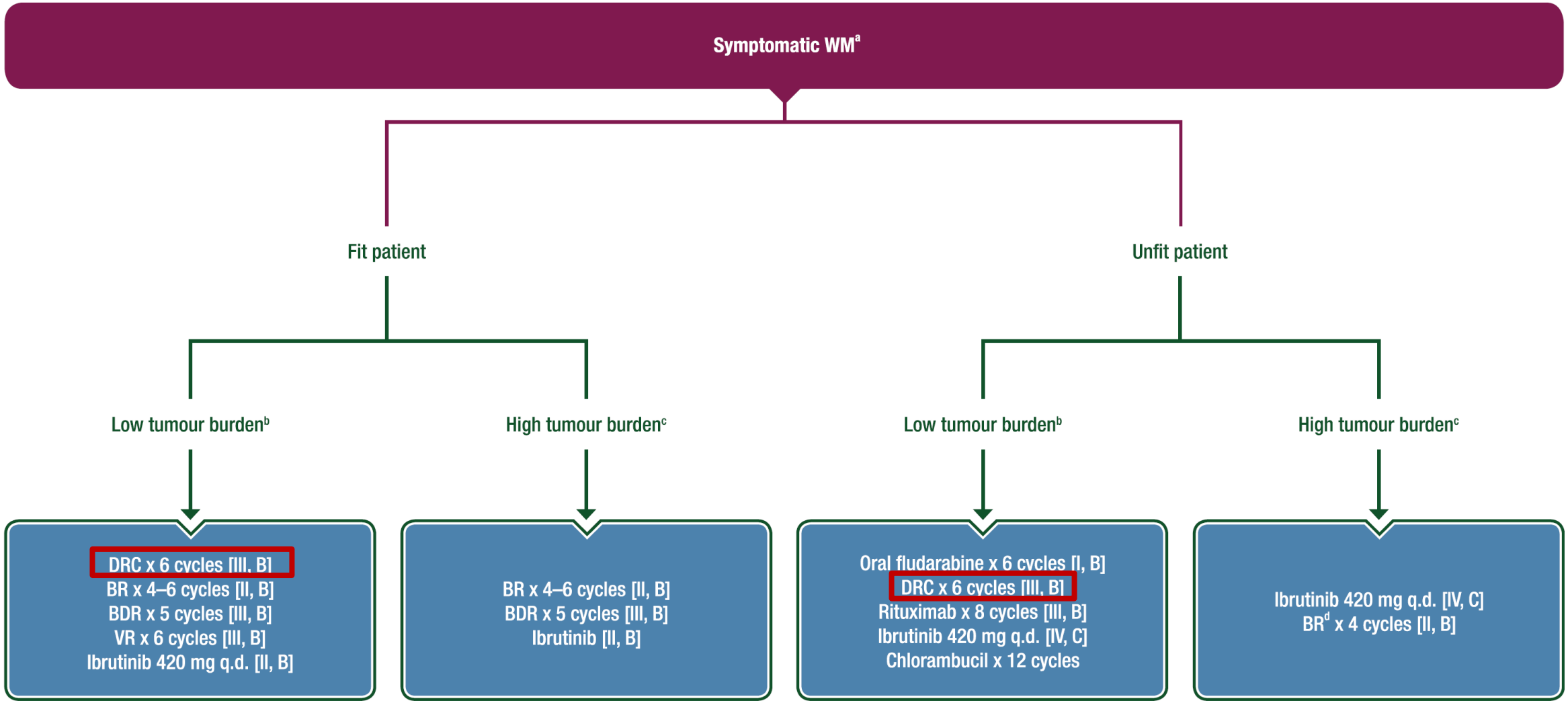
Treatment

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

Waldenstroem
ESMO/EHA Guidelines (Erstlinie)



Kastritis, Ann Oncol 2018;29:iv41-50

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

Primary Endpoint: 1-year PFS

Sponsor: Ulm
Participating countries: Germany, Greece, France
Activated: actively recruiting

41 von 53 Patienten eingeschlossen

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

Sponsor: Ulm
Participating countries: pan-European
Activation: Q1 2021

Studien in Indolenten Lymphomen
Take home messages 2021

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- **Follikuläres Lymphom:**
  - Frühe Stadien: Radiatio (2, 24 Gray) + AK (Rit, Obi)
  - Erstlinie: Chemo-freie Konzepte (Alternative C: Copanlisib)
  - Rezidiv: Ritux-Len, vs. Tazemetostat, CD19-AK, bispezifische AK

- **Marginalzonen-Lymphom:**
  - Erstlinie: AK (Rit, Obi) +/- targeted Tx
  - Rezidive: targeted Tx +/- AK

- **Waldenstroem:**
  - Erstlinie: Chemo-freie Konzepte (Ibrutinib: ECWM-2, ECWM-3)
  - Rezidv: Ibrutinib-Kombinationen (CZAR-1)

GLA/European MCL Network

Acknowledgements