17TH ULTMANN
CHICAGO LYMPHOMA SYMPOSIUM

THE UNIVERSITY OF CHICAGO
MEDICINE & BIOLOGICAL SCIENCES

17TH INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

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chicagolymphoma.com

Relevant Disclosures

Genentech – Research Funding, Consulting

Celgene (BMS)– Research Funding, Consulting

Follicular Lymphoma:
Treatment of Newly Diagnosed Disease

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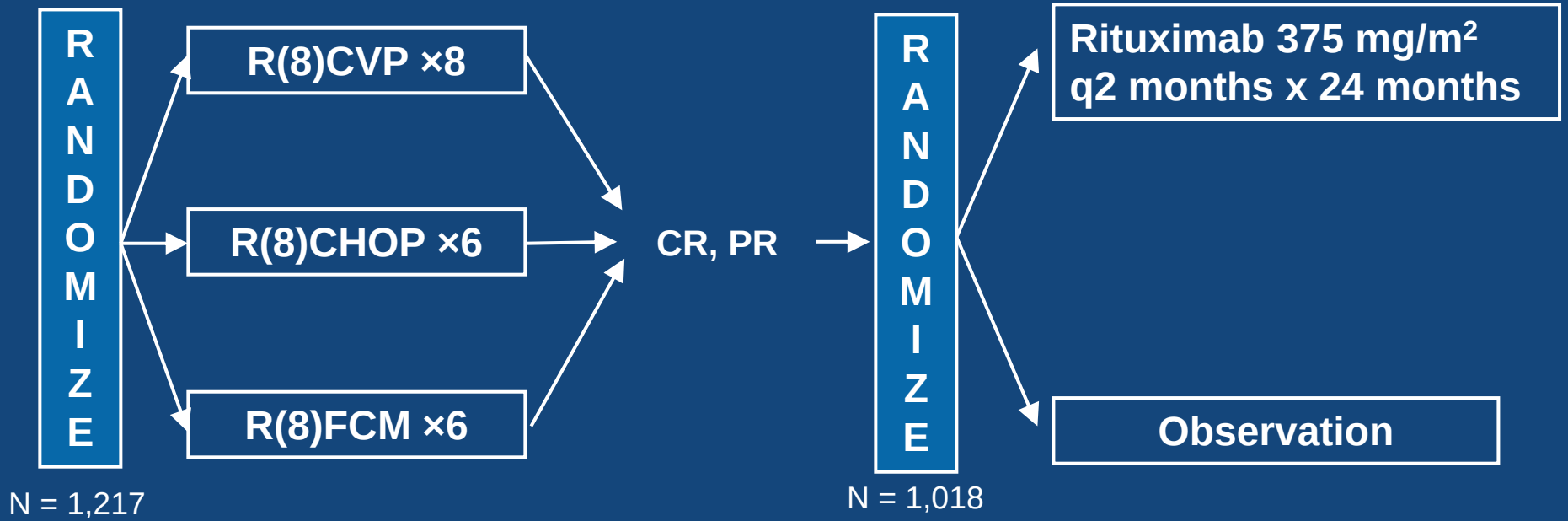
Follicular Lymphoma

- Generally indolent disease.
- Watchful waiting/active surveillance initially appropriate for asymptomatic patients with low tumor burden.
- Common Indication for Treatment: GELF*Criteria:
  - Three nodes in three distinct areas, with each ≥3 cm
  - Tumor ≥7 cm
  - Symptomatic splenomegaly
  - Ascites or pleural effusion
  - Cytopenias
  - Leukemic phase disease (rare)

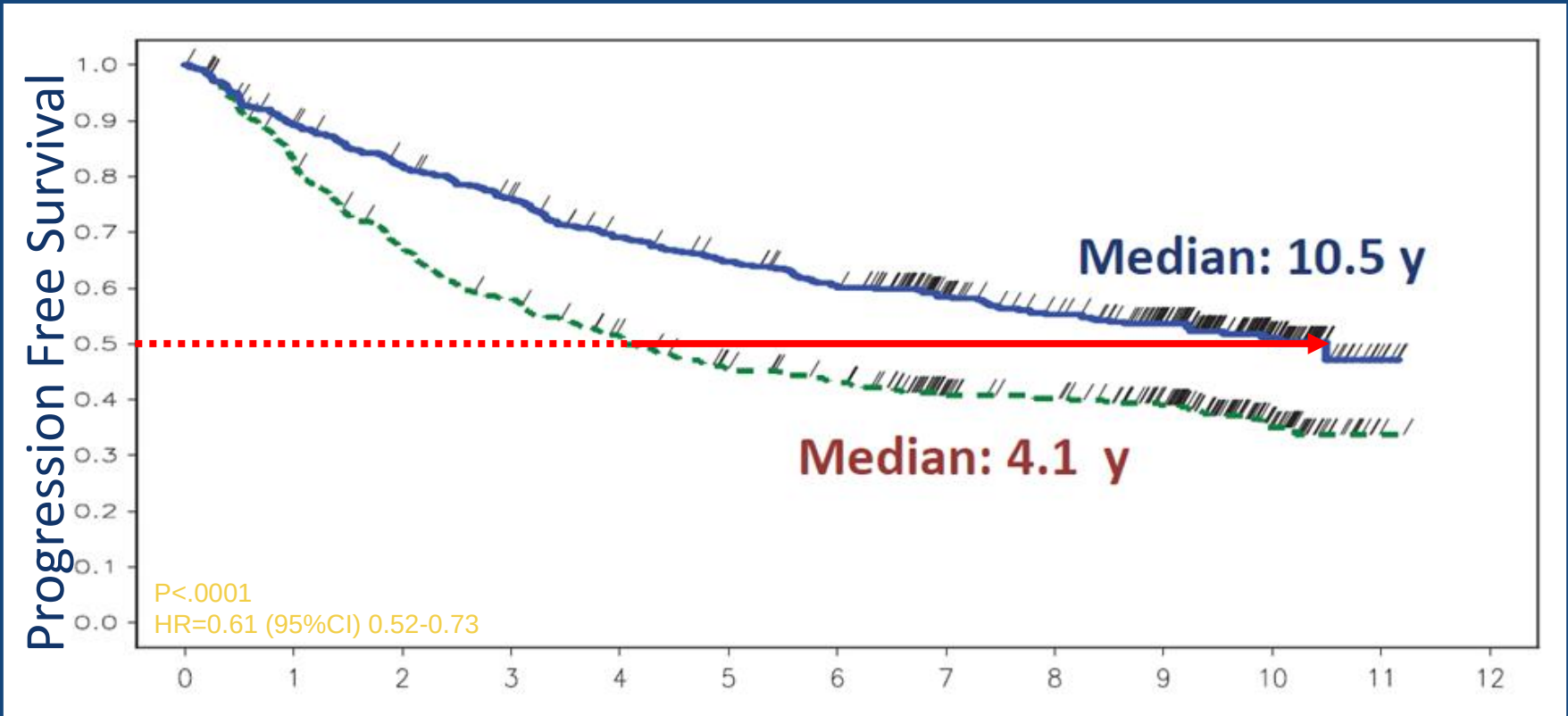
*GELF = Groupe d'Etude des Lymphomes Folliculaires

The PRIMA Trial
Study Design

- Previously untreated
- Grade 1, 2, 3a follicular lymphoma
- High tumor burden (GELF criteria)



The PRIMA Trial
Long-Term Follow-up



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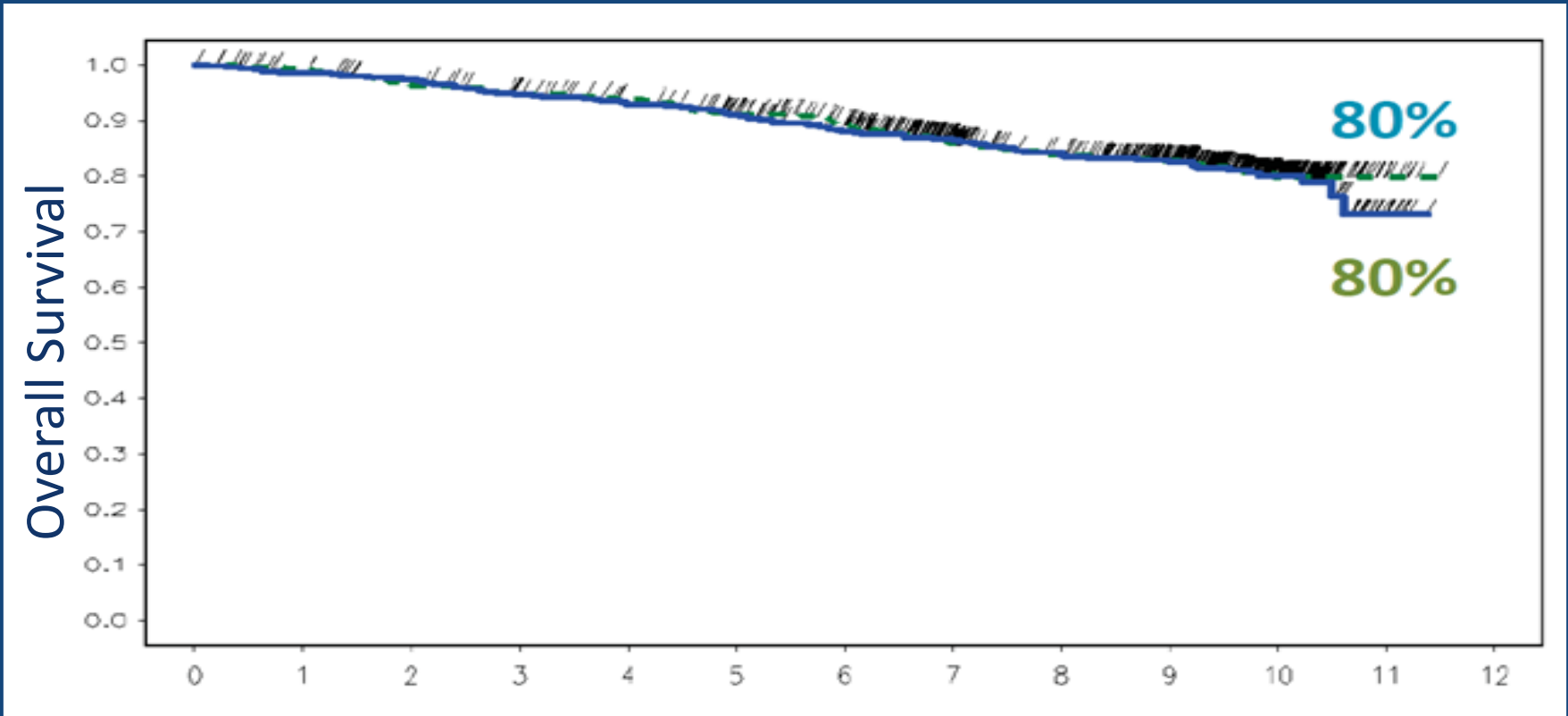
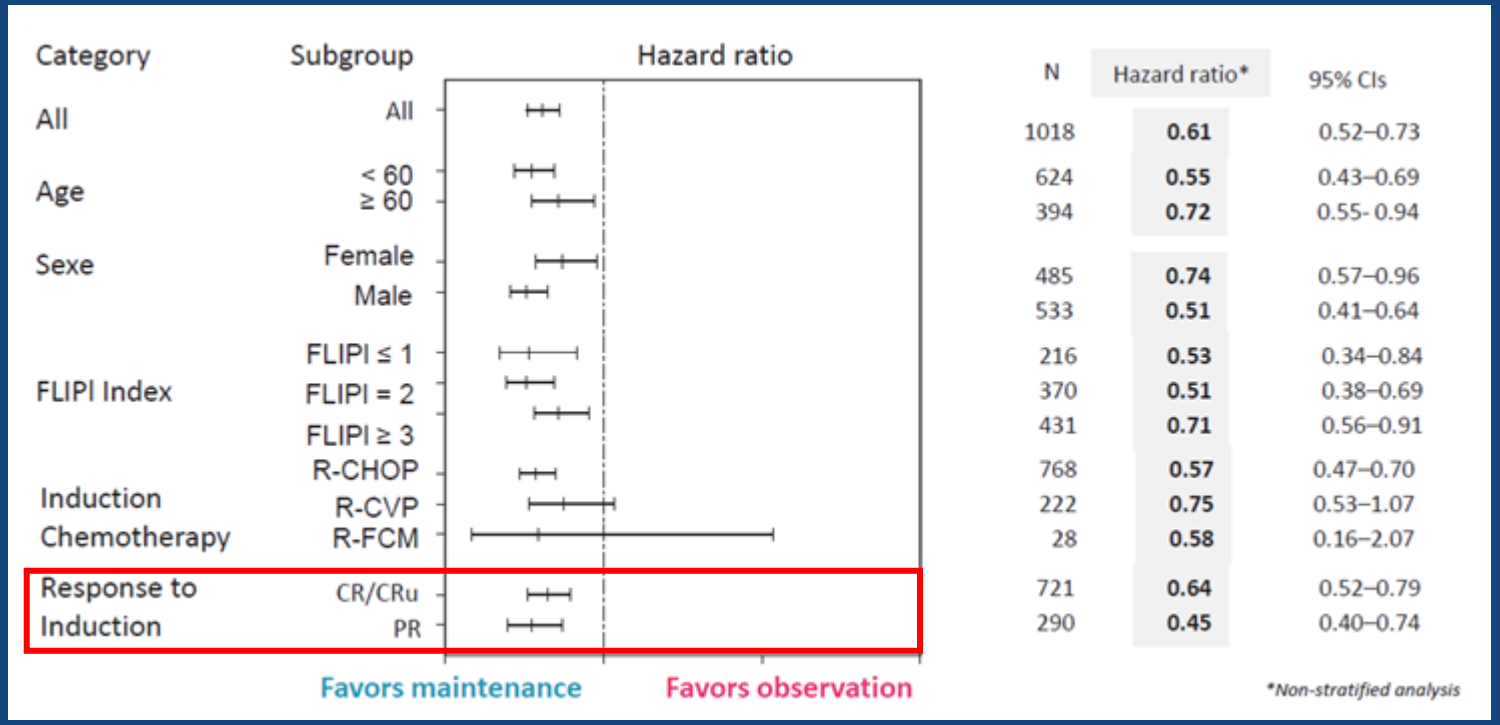


The PRIMA Trial
Rituximab Maintenance in Major Subgroups



Category	Subgroup	N	Hazard ratio*	95% CIs
All	All	1018	**0.61**	0.52–0.73
Age	< 60	624	**0.55**	0.43–0.69
	≥ 60	394	**0.72**	0.55- 0.94
Sexe	Female	485	**0.74**	0.57–0.96
	Male	533	**0.51**	0.41–0.64
FLIPI Index	FLIPI ≤ 1	216	**0.53**	0.34–0.84
	FLIPI = 2	370	**0.51**	0.38–0.69
	FLIPI ≥ 3	431	**0.71**	0.56–0.91
Induction Chemotherapy	R-CHOP	768	**0.57**	0.47–0.70
	R-CVP	222	**0.75**	0.53–1.07
	R-FCM	28	**0.58**	0.16–2.07
Response to Induction	CR/CRu	721	**0.64**	0.52–0.79
	PR	290	**0.45**	0.40–0.74

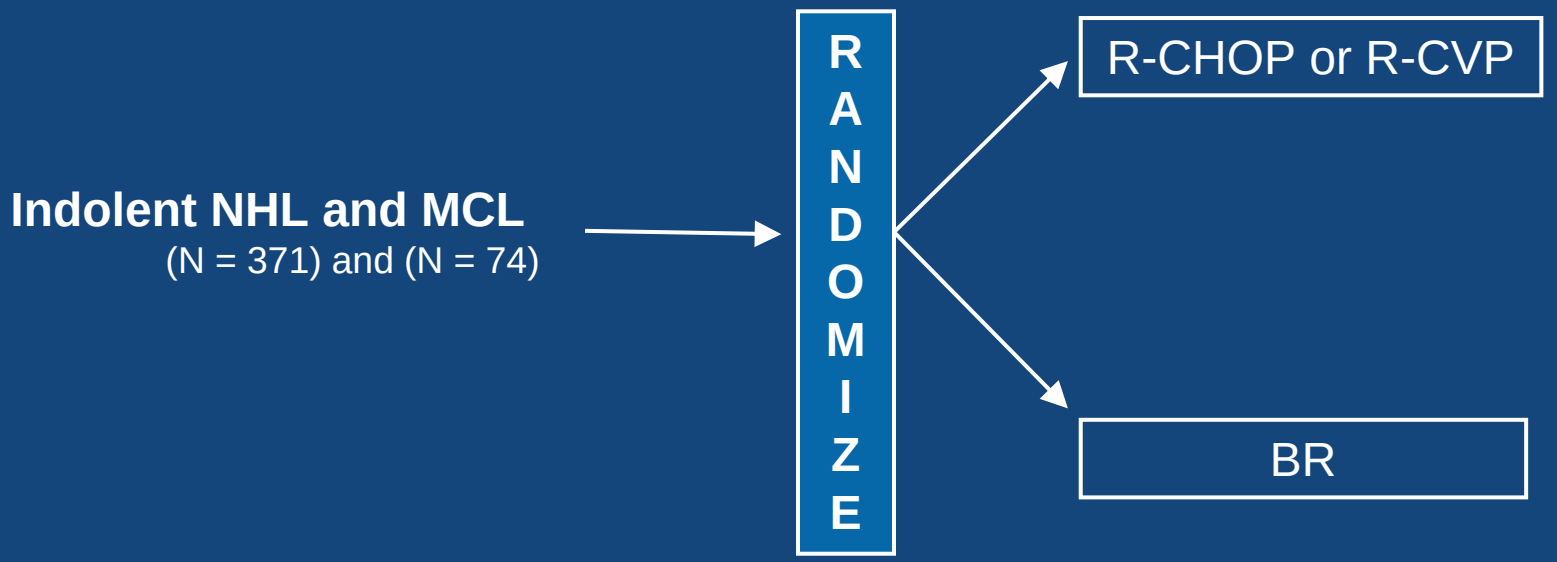
*Non-stratified analysis

The PRIMA Trial
Rituximab Maintenance in Major Subgroups

Safety Parameter	Observation N = 508	Rituximab Maintenance N = 501
Adverse events (includes Grade 3–5 toxicities, Grade 2–5 infections, and serious AEs)	194 (38%)	285 (57%)
Grade 3/4 adverse events	**86 (17%)**	**122 (24%) ***
Serious adverse events	**68 (13%)**	**106 (21%)**
Total deaths	83 (16%)	84 (17%)
Grade 5 AEs	3 (<1%)	8 (2%)

* Difference essentially represented by neutropenia and infections

BRIGHT TRIAL:
R-CHOP/R-CVP vs. BR



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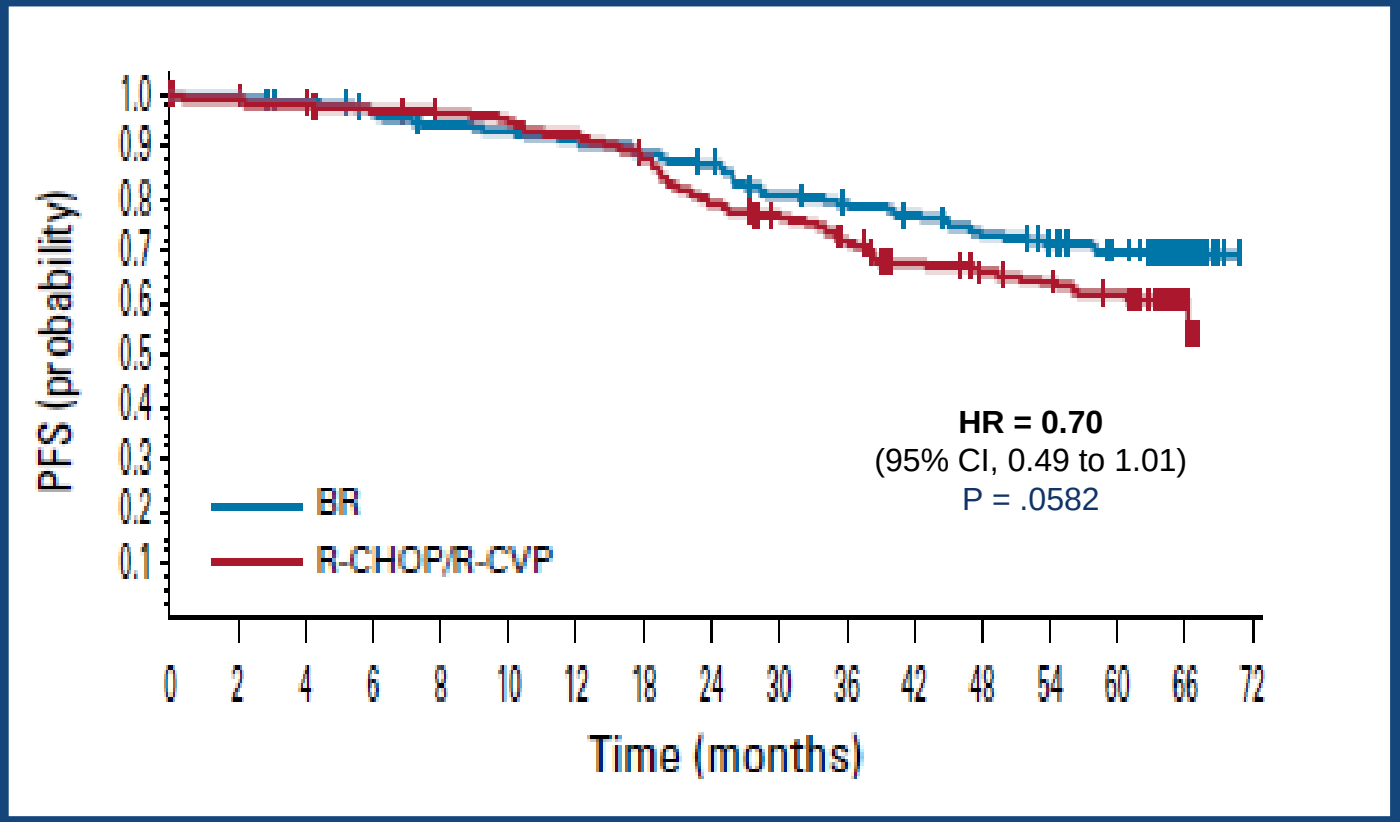
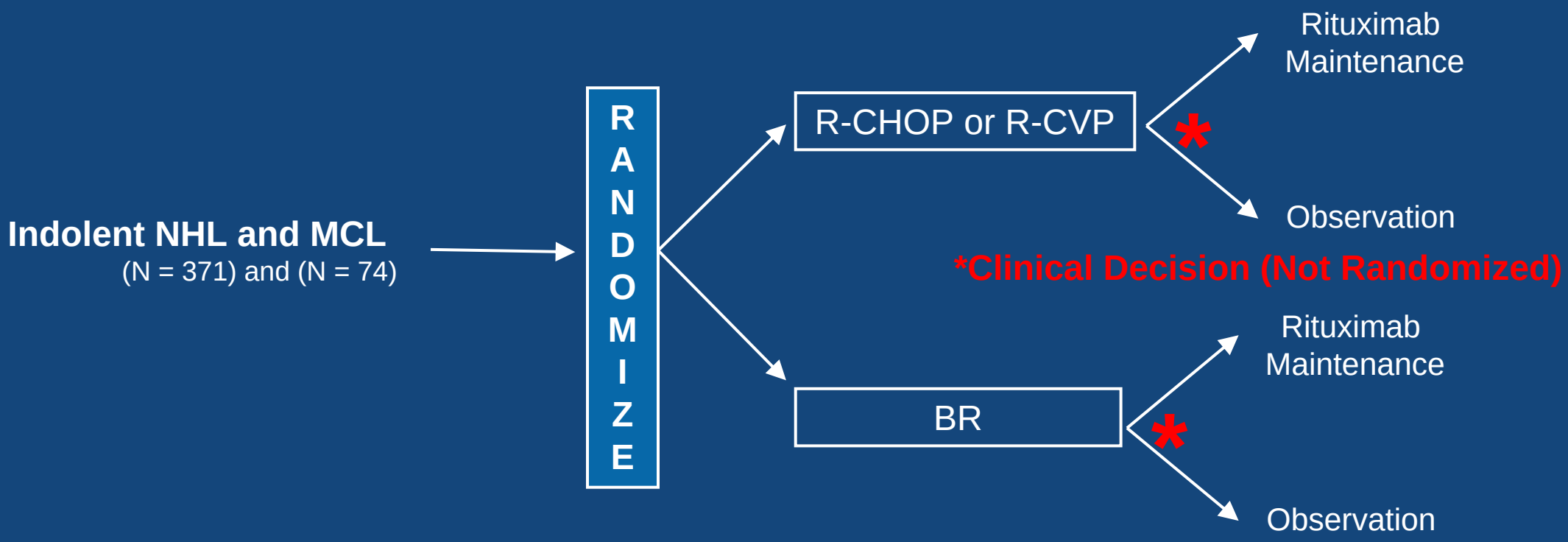


BRIGHT TRIAL:
R-CHOP/R-CVP vs. BR - Impact of Post-Study Treatment



BRIGHT TRIAL:
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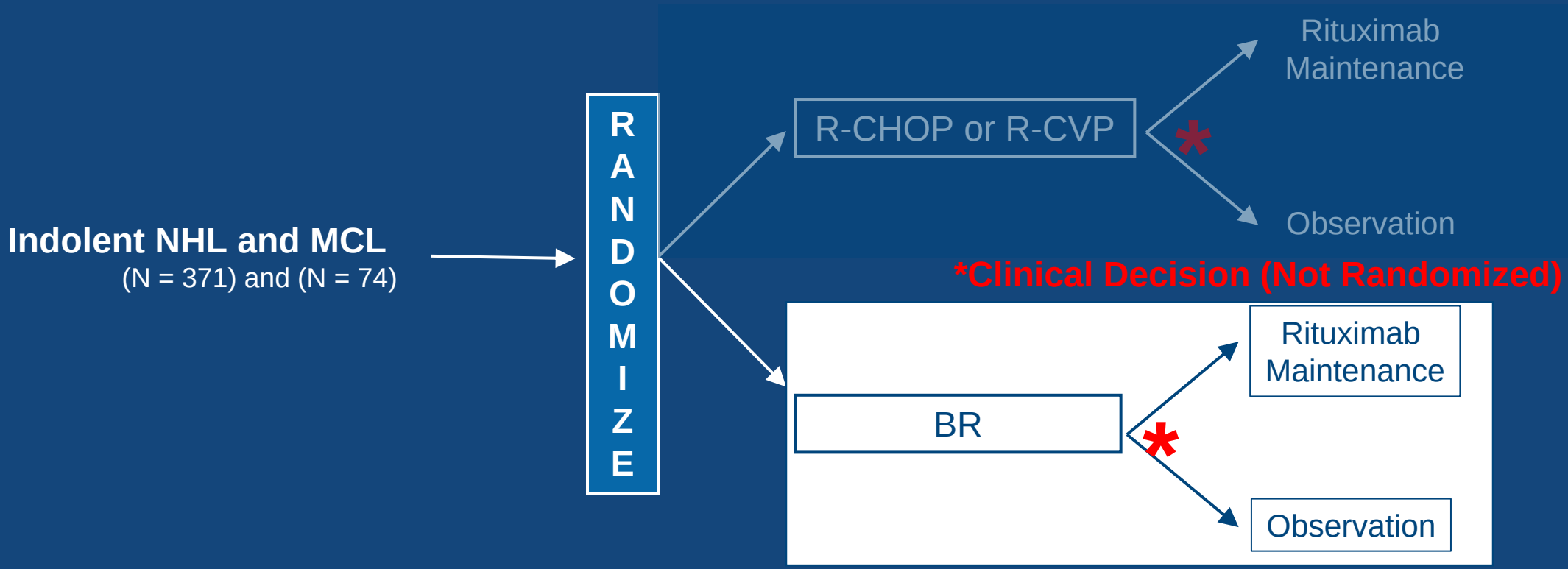
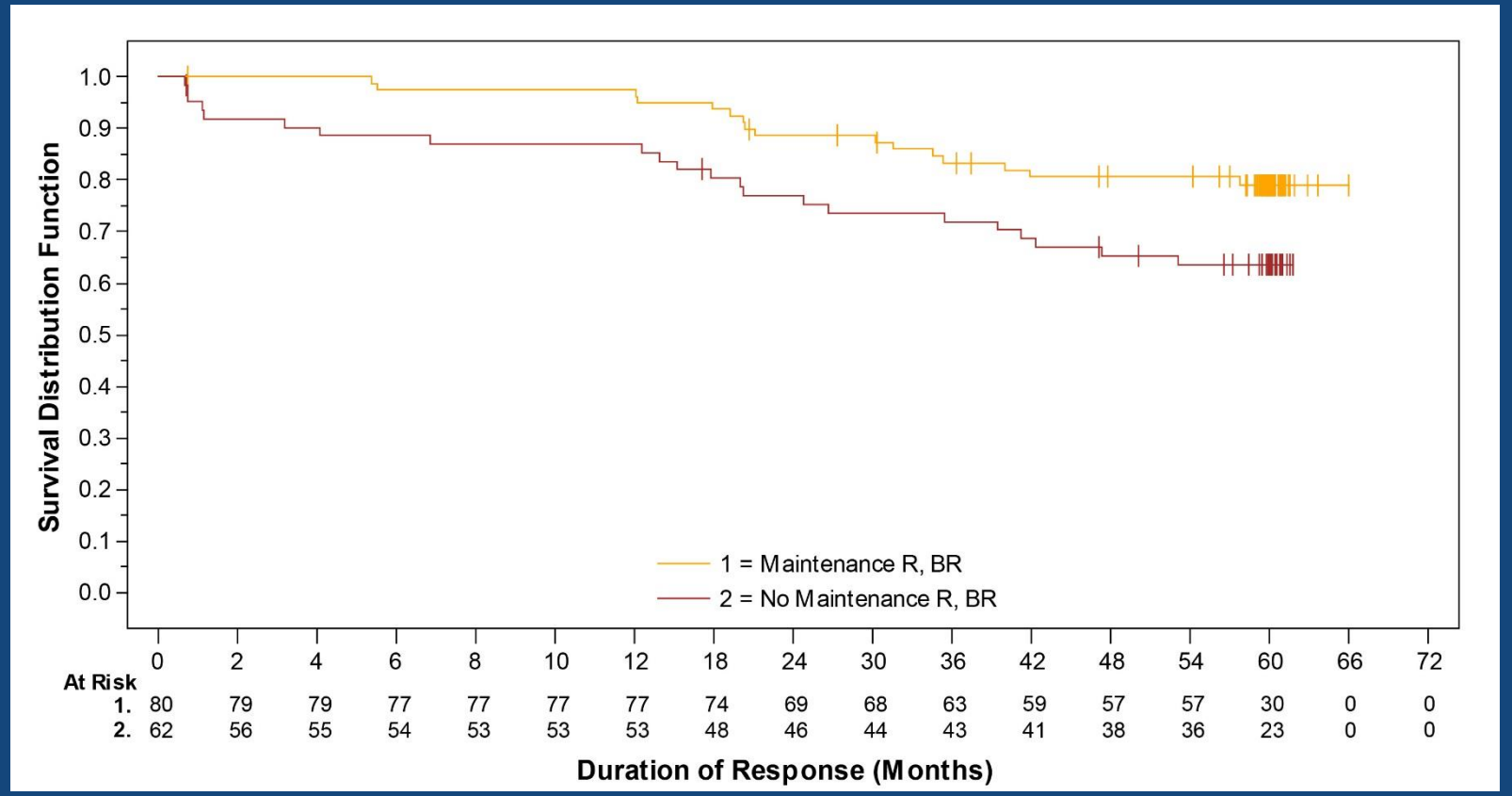


BRIGHT TRIAL:
Adverse Events During Induction*

n (%)	BR (n = 144)	
	Maintenance R (n = 81)	No Maintenance R (n = 63)
Any adverse event	81 (100)	63 (100)
Grade ≥3 adverse event	48 (59)	35 (56)
Serious adverse events (SAEs)	19 (23)	20 (32)
SAEs occurring in >2 patients		
Febrile neutropenia	3 (4)	1 (2)
Neutropenia	3 (4)	0
Pyrexia	1 (1)	4 (6)
Pneumonia	1 (1)	3 (5)
SAEs of interest by SOC		
Infections and infestations	5 (6)	8 (13)
Secondary malignancies	0	1 (2)

*Adverse events were only collected during BR or R-CHOP/R-CVP study period, and not during maintenance therapy or long-term follow-up. Includes FL patients with CR or PR.

BRIGHT TRIAL:
Maintenance for FL Patients in CR or PR after BR induction



Real World Experience

Maintenance Rituximab or Observation after Frontline Treatment with Bendamustine-Rituximab (BR) for Follicular Lymphoma

Brian T. Hill, MD, PhD Loretta Nastoupil, MD, Allison M. Winter, MD, Melody R Becnel, MD, James R. Cerhan, MD, PhD, Thomas M Habermann, MD, Brian K Link, MD, Matthew J Maurer, MS, Bita Fakhri, MD, MPH, Prathima Reddy, MD, Stephen D. Smith, MD, Dhruvika Mukhija, MD, Deepa Jagadeesh, MD, MPH, Amrita Desai, MD, Juan Pablo Alderuccio, MD, Izidore S Lossos, MD, Pooja Mehra, MD, Craig A. Portell, MD, Max L. Goldman, BA, Oscar Calzada, BS, Jonathon B Cohen, MD, MS, Mohammad Junaid Hussain, MD, Nilanjan Ghosh, MD, PhD, Paolo Caimi, MD, Timothy Tiutan, MD, Peter Martin, FRCPC, MD, MS, Abhigna Kodali, MD, Andrew M Evens, DO, MSc and Brad S Kahl, MD

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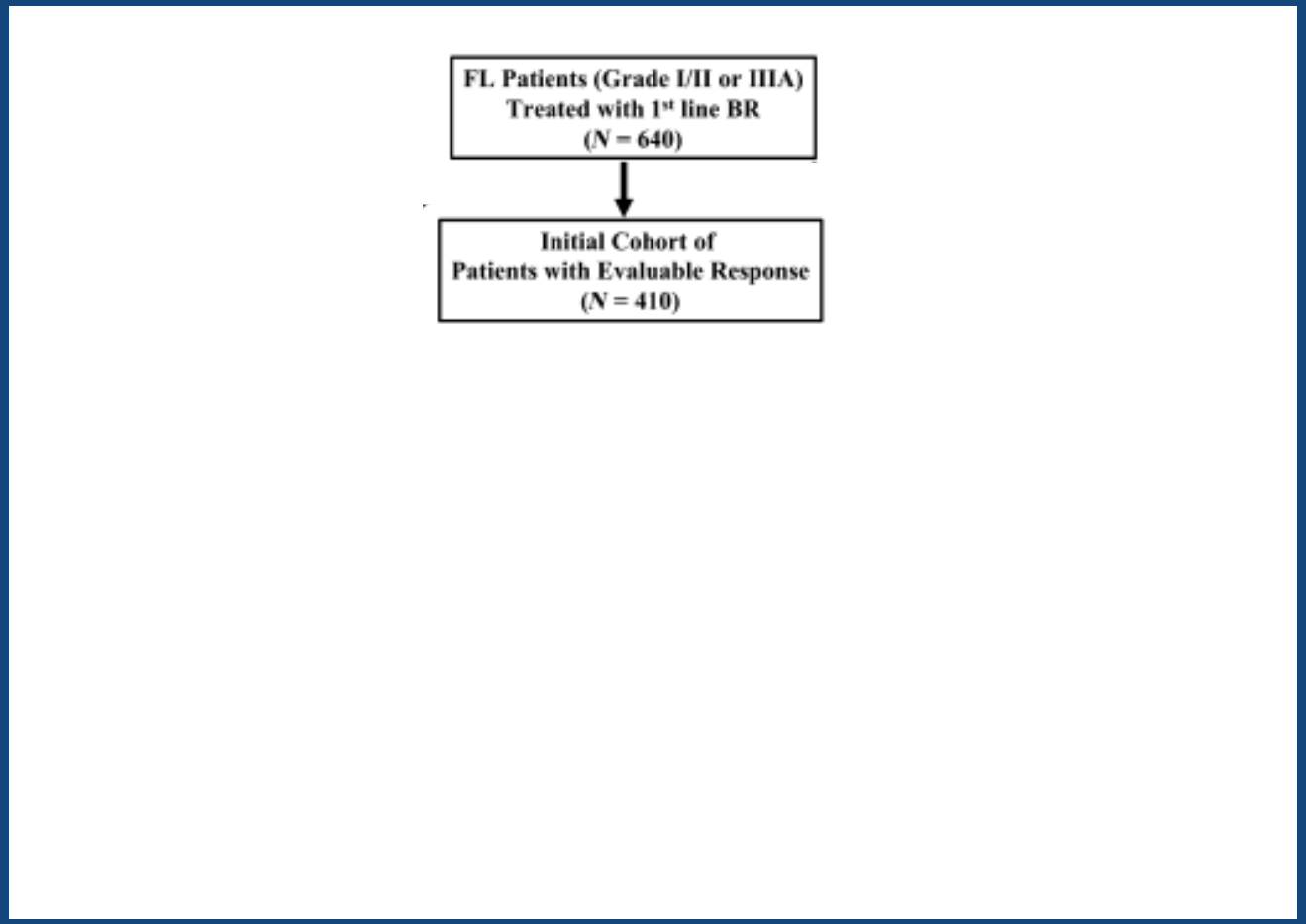

Hill, et al BJH, 2019

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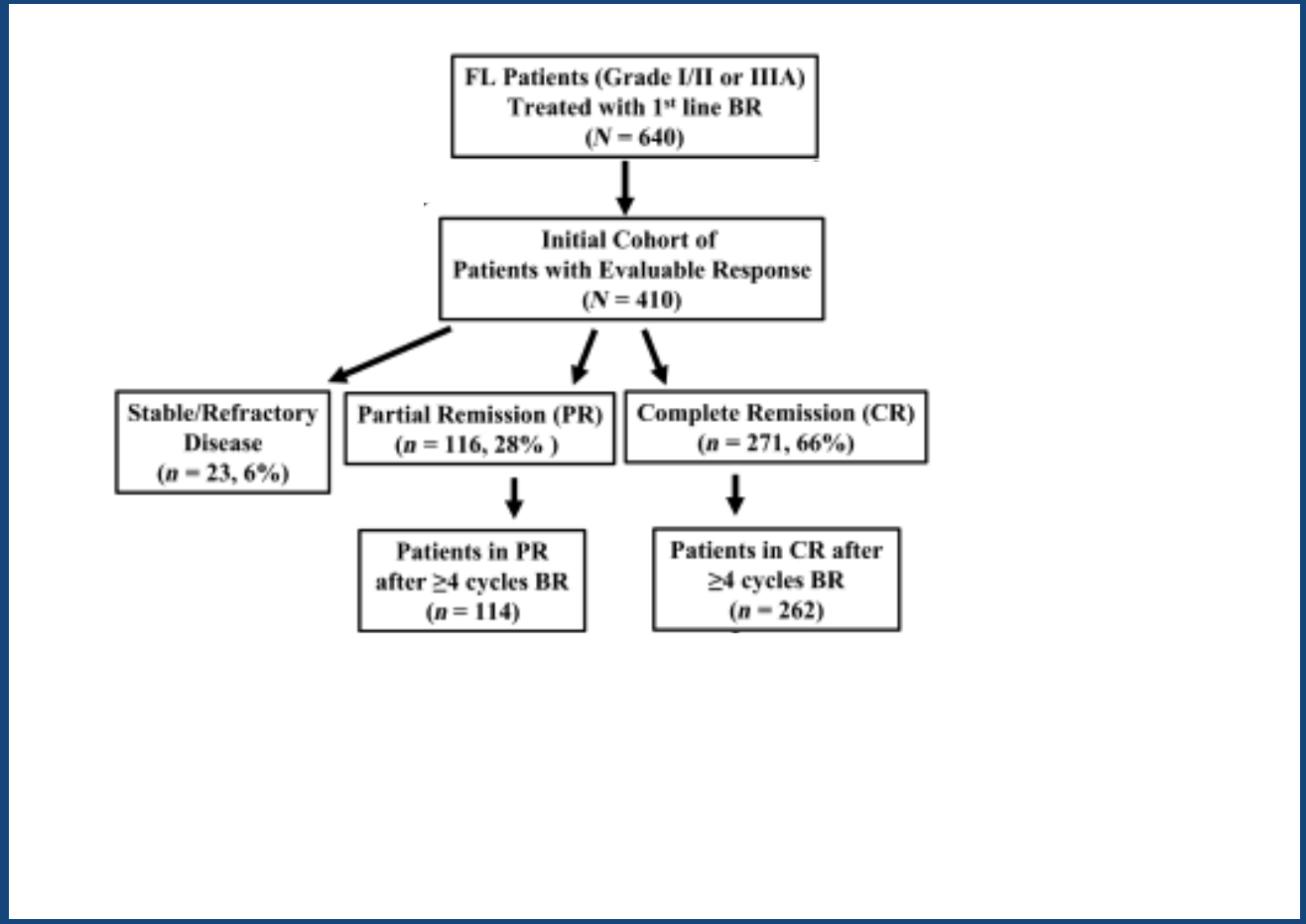

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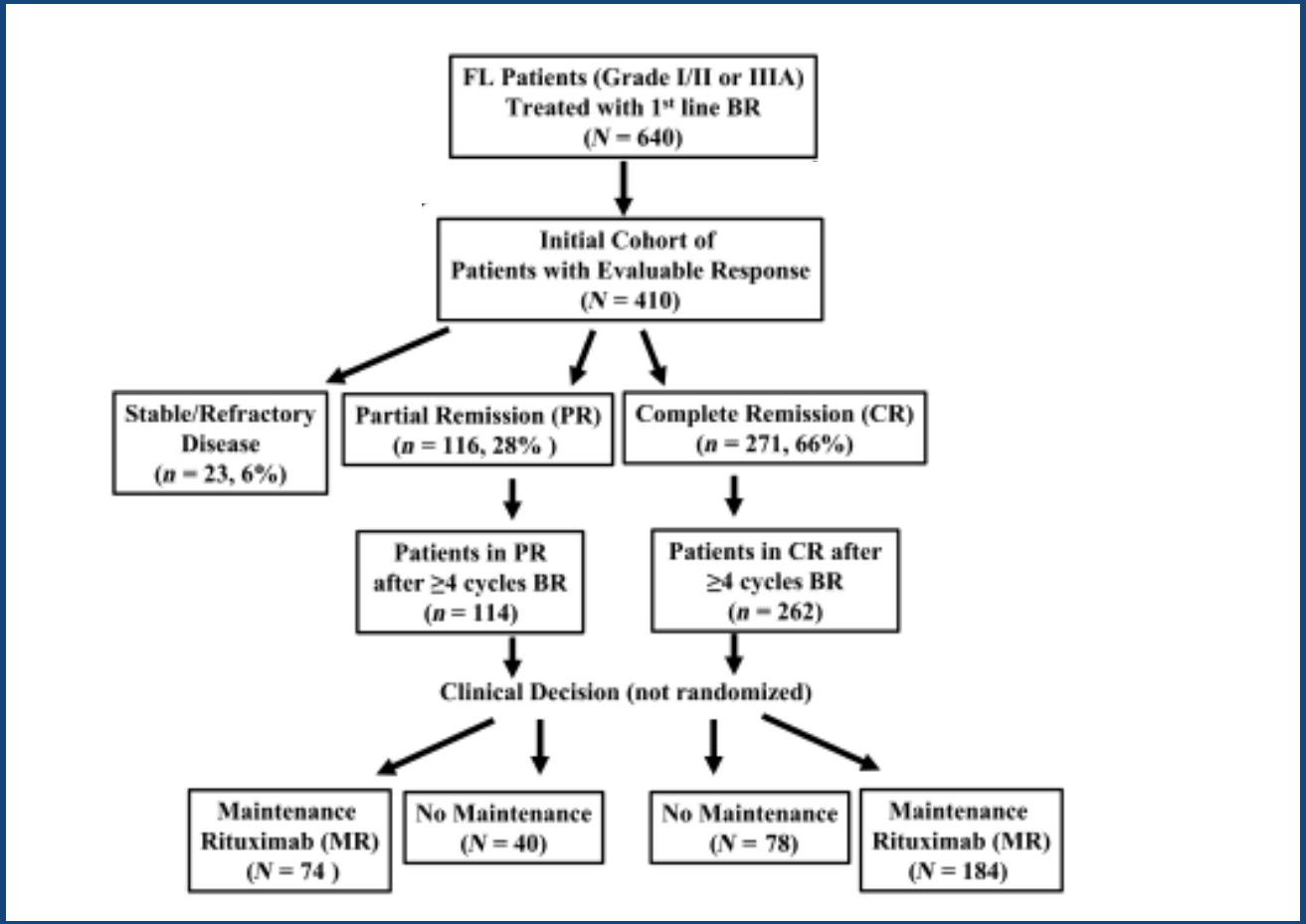
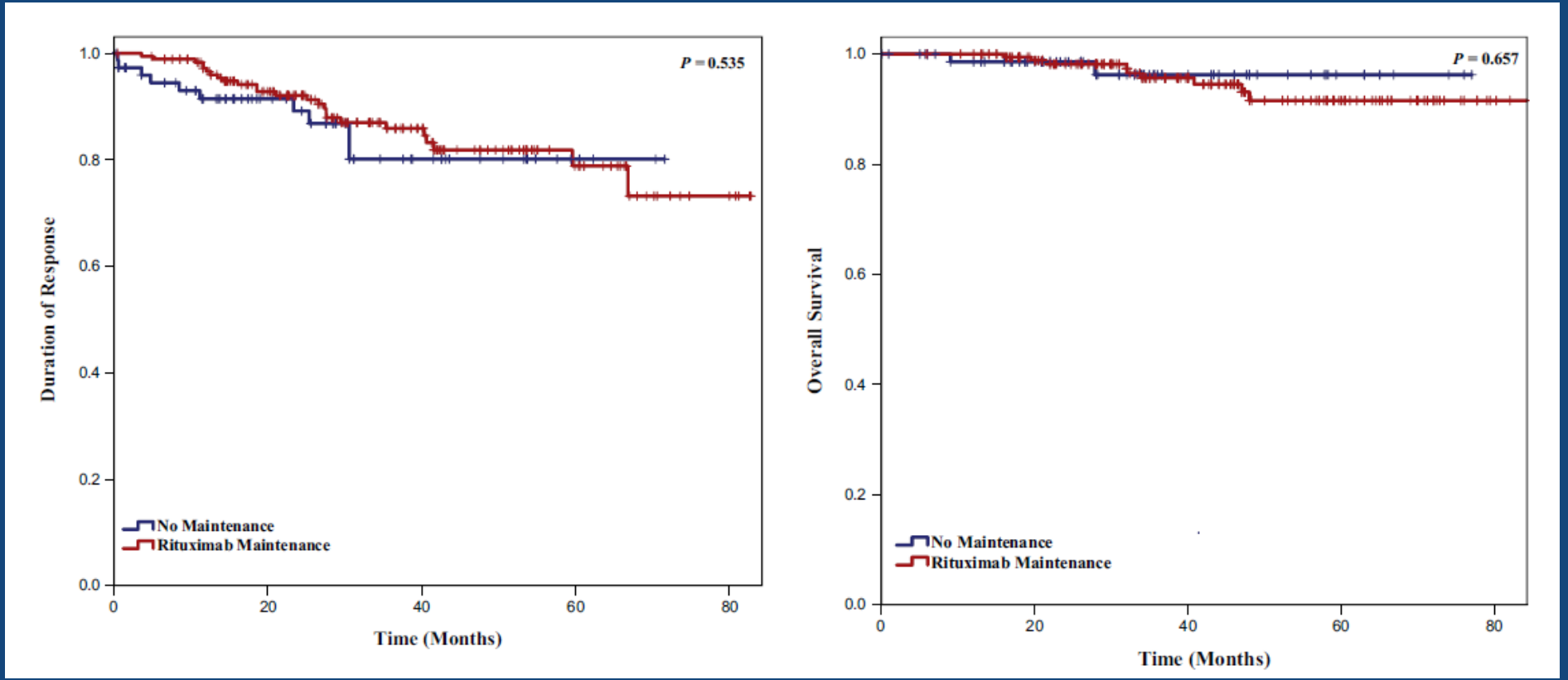


Real World Experience

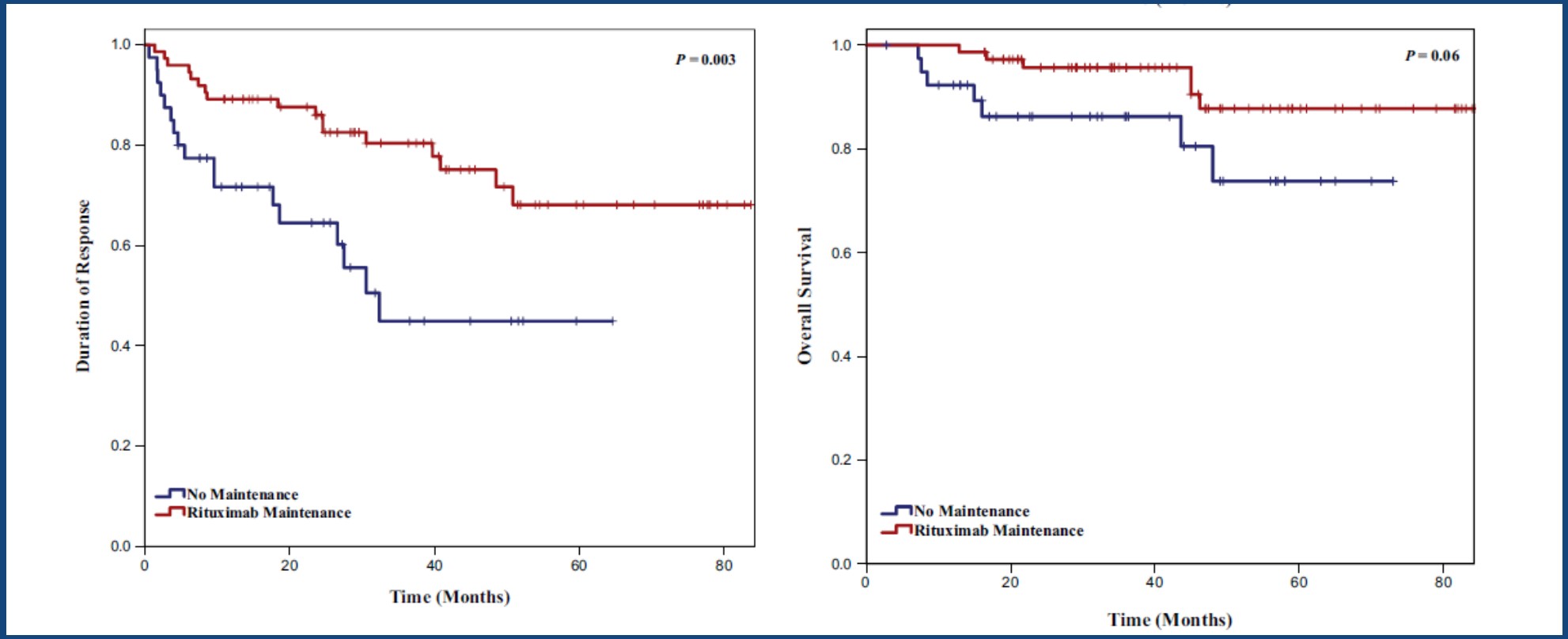
No Benefit to Maintenance For Patients in Complete Remission (CR) after BR



Hill, et al BJH, 2019

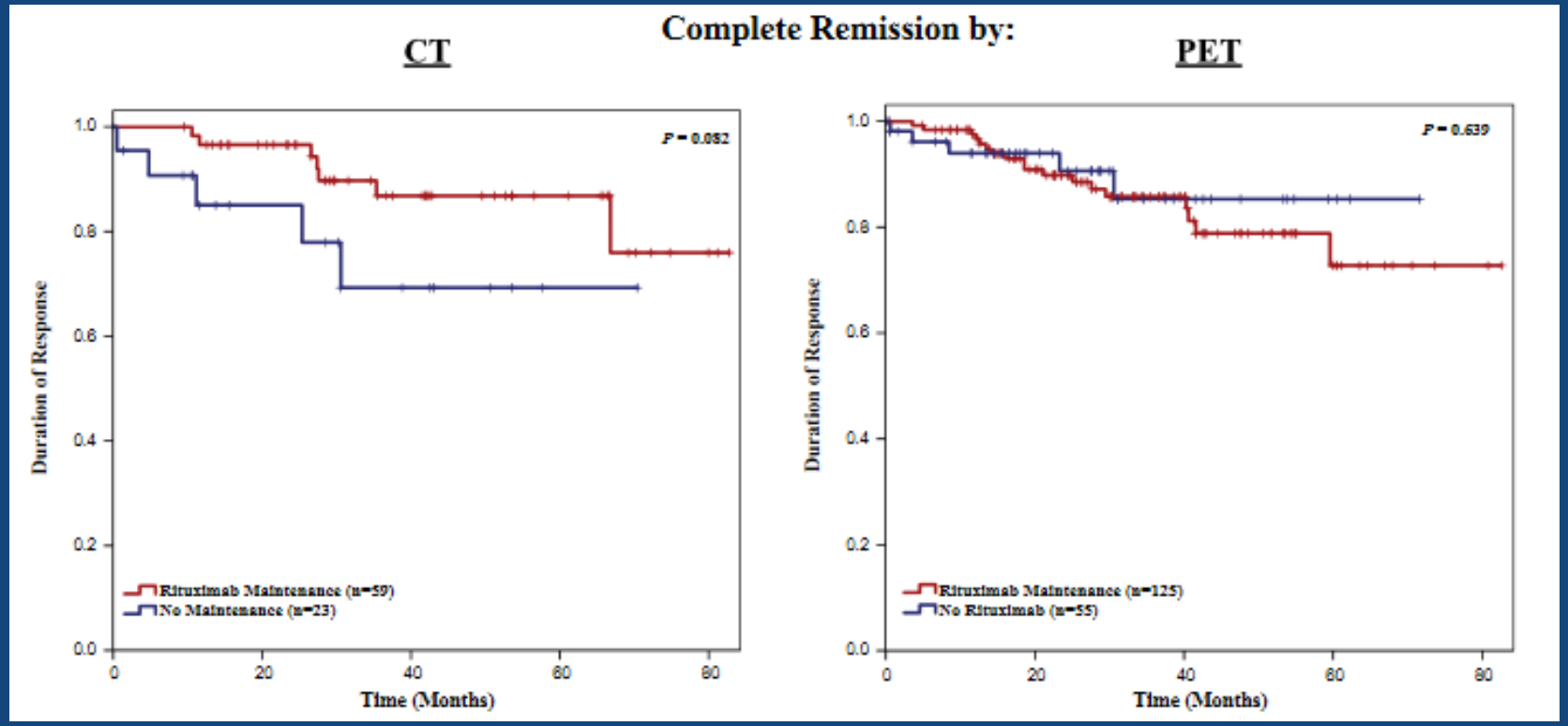
Real World Experience

PFS Benefit for Patients in Partial Remission (PR) after BR



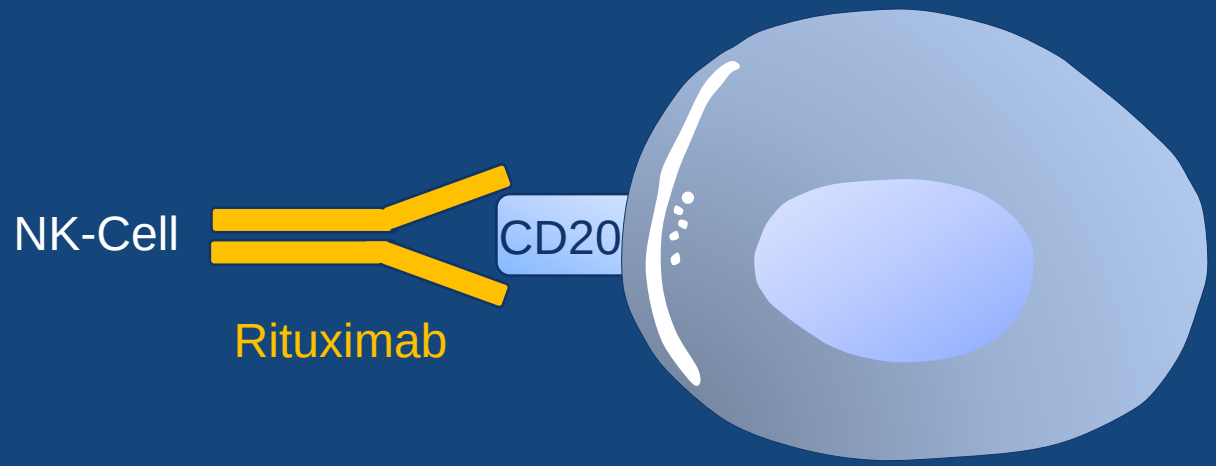
Real World Experience

Potential Role of PET for CR Patients not Likely to Benefit from Maintenance.



Role of anti-CD20 Monoclonal Antibody

Obinituzumab – a more potent agent in FL?

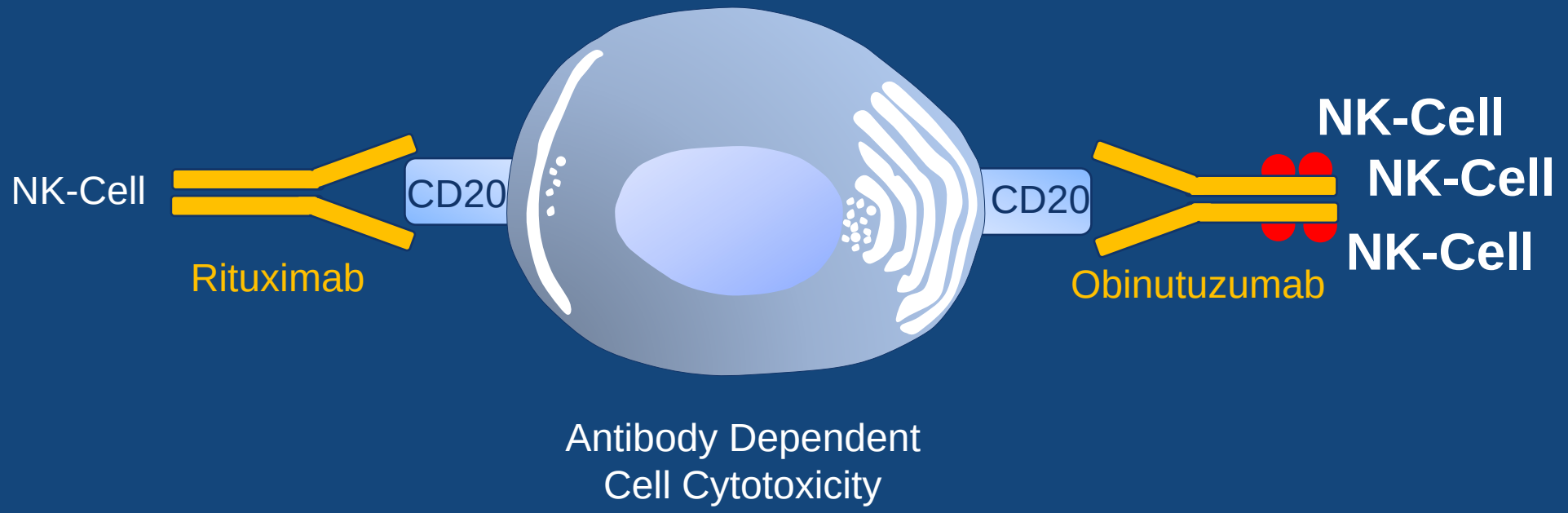


Antibody Dependent
Cell Cytotoxicity

Glycoslyation

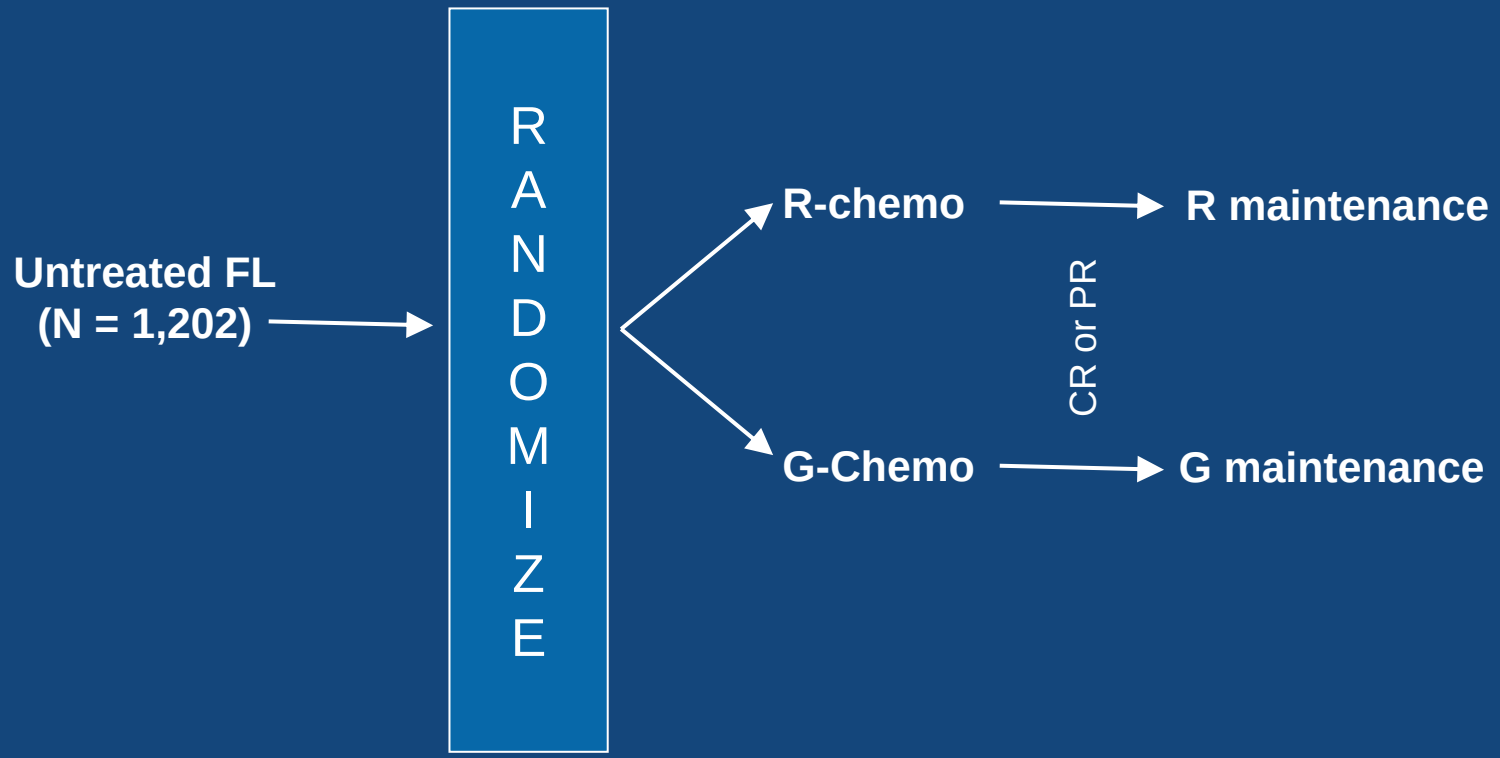
Role of anti-CD20 Monoclonal Antibody

Obinituzumab – a more potent agent in FL?



GALLIUM

Chemotherapy + Rituximab (R) vs. Obinutuzumab (G) for Untreated FL



Marcus, et al NEJM, 2017

GALLIUM

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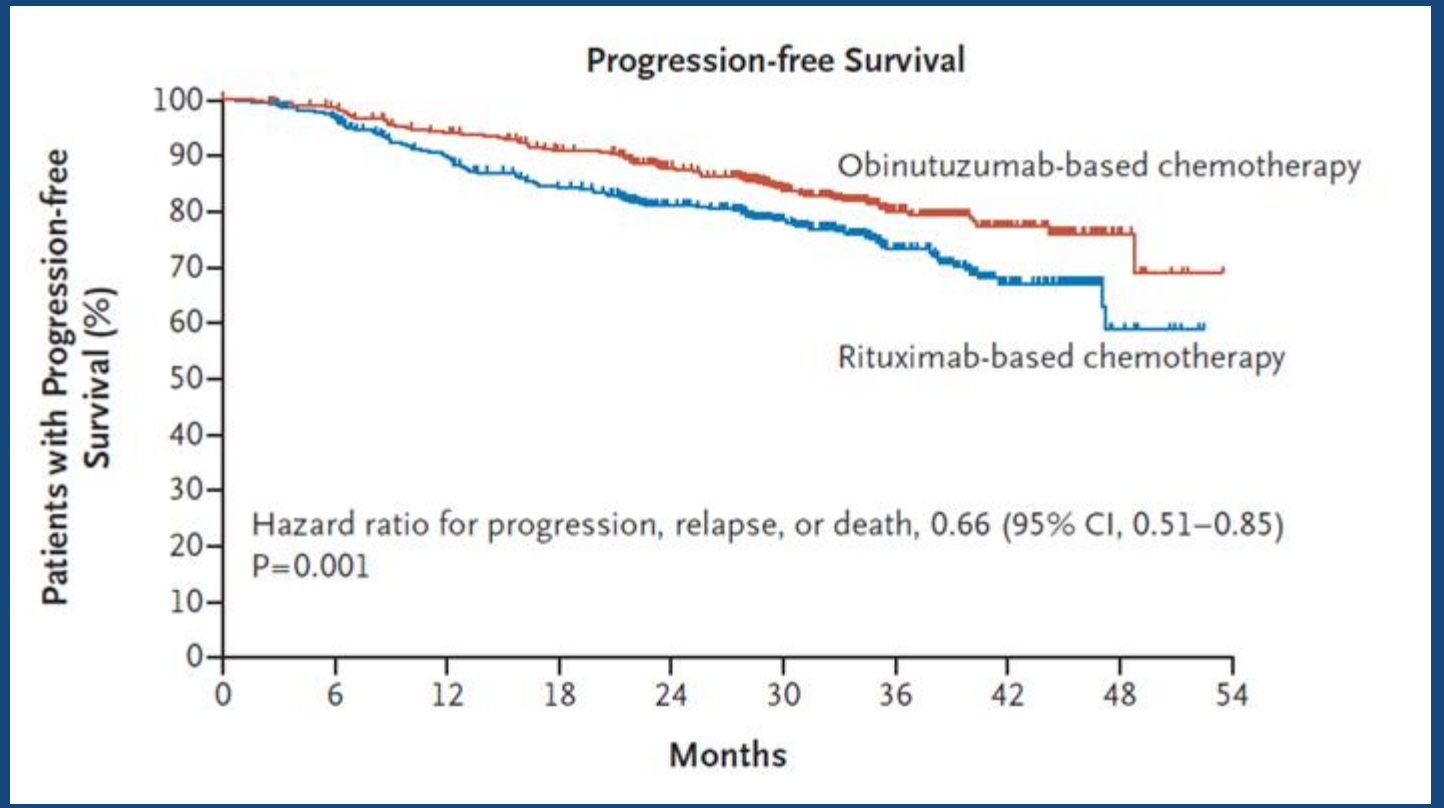
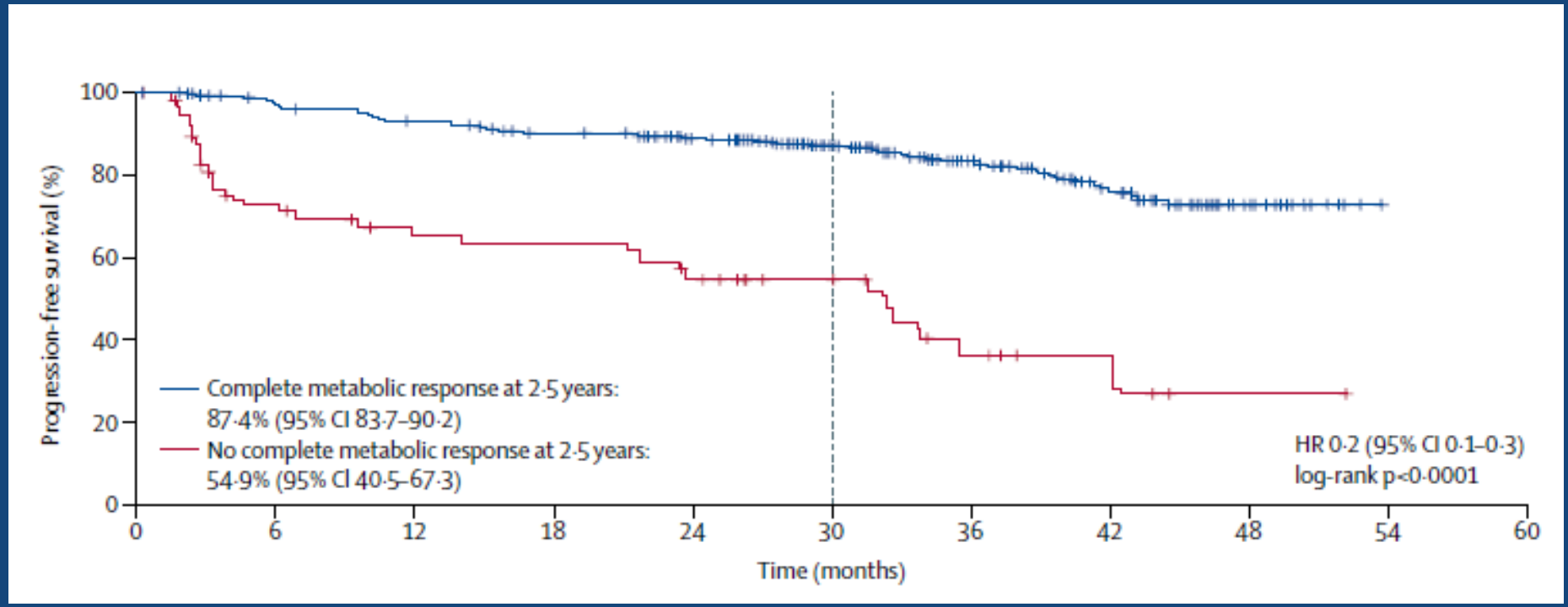


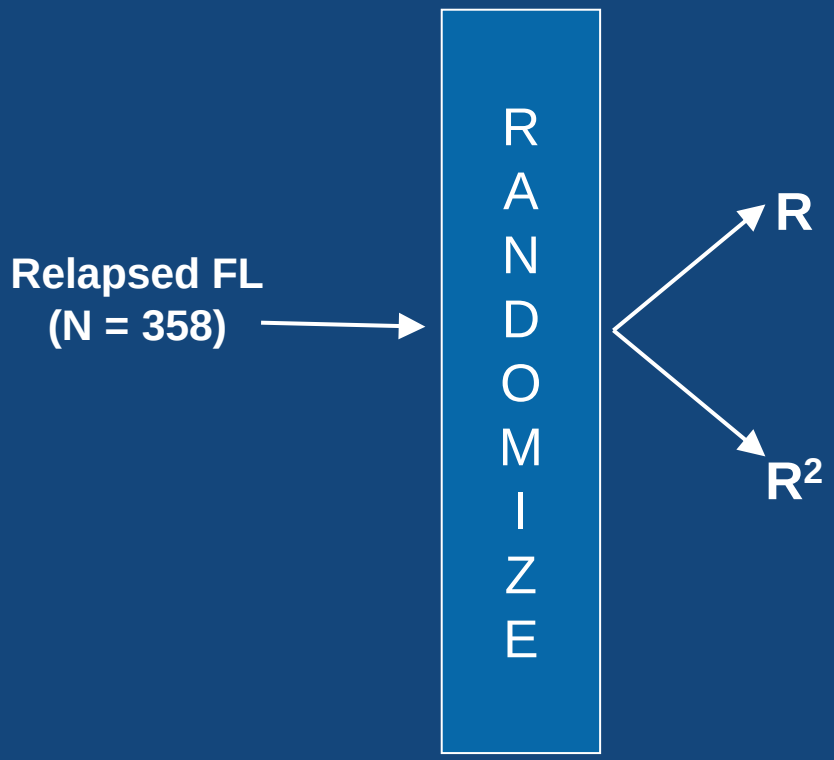
GALLIUM

Role of End-of-Treatment PET in Predicting PFS



Maintenance Beyond anti-CD20 mAb

AUGMENT Trial: Rituximab (R) vs. Lenalidomide + R (R^2) for Relapsed FL



Leonard, et al, JCO, 2018

Maintenance Beyond anti-CD20 mAb

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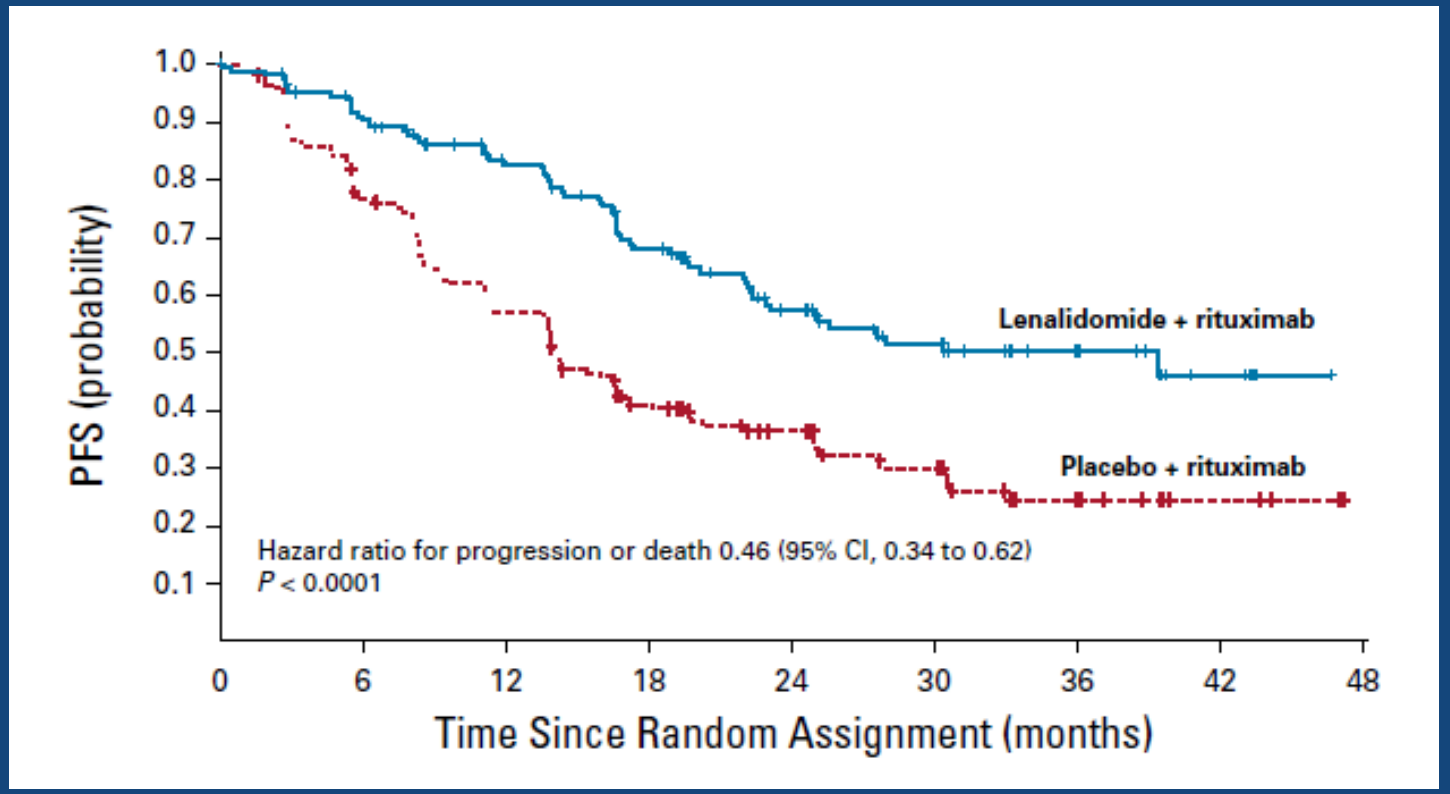
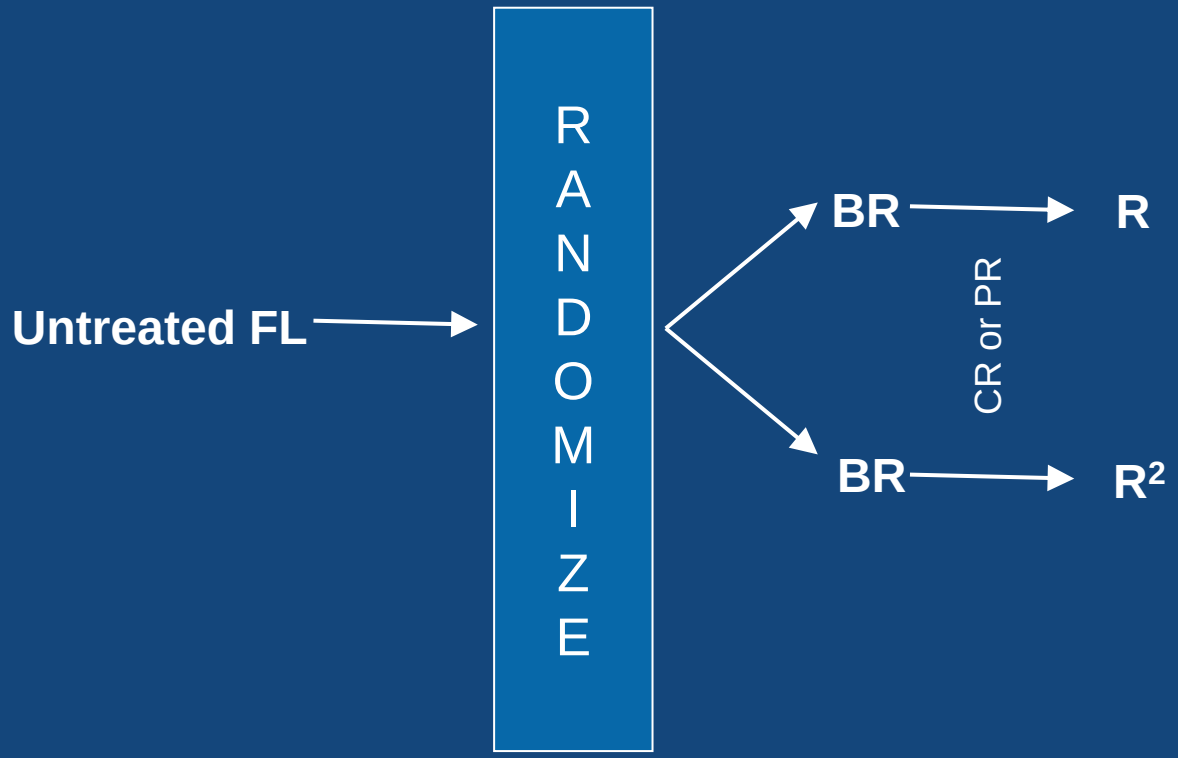


Maintenance Beyond anti-CD20 mAb

E2408 Trial: R vs. R^2 after BR for frontline FL



*3rd arm: BR + Bortezomib followed by R

ECOG-ACRIN cancer research group
Reshaping the future of patient care

Summary

- PRIMA study showed similar benefit to maintenance therapy for all patients responding to R-CHOP, but no randomized prospective trials address role of maintenance after BR.
- Post-hoc analysis of BRIGHT and Real World Experience Data suggest improvement in PFS with maintenance after BR, possibly restricted for patients with < complete remission.
- PET scan is a powerful predictor of PFS at end-of-induction after chemoimmunotherapy.
- Obinutuzumab improves proportion of PET negativity vs. rituximab.
- Addition of lenalidomide to R (R^2) improves PFS in relapsed FL. Data for R^2 after frontline chemoimmunotherapy with BR are expected soon.