Front-line treatment in young patients with MCL: Role of maintenance therapy

Rome 2017

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CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

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THE LYMPHOMA STUDY ASSOCIATION

- Is there a need for maintenance for young MCL patients ?
- Does maintenance after ASCT prolong PFS, EFS and/or OS ?
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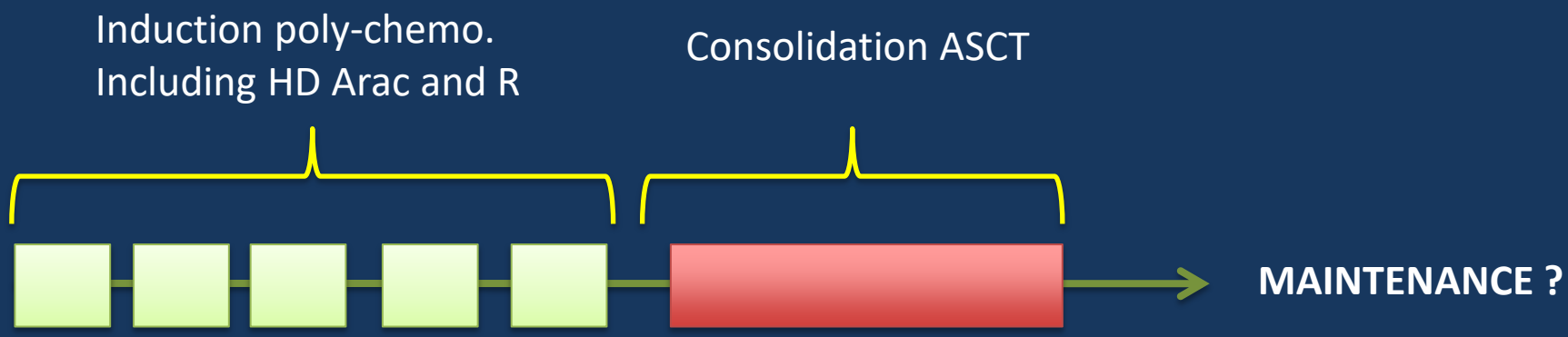
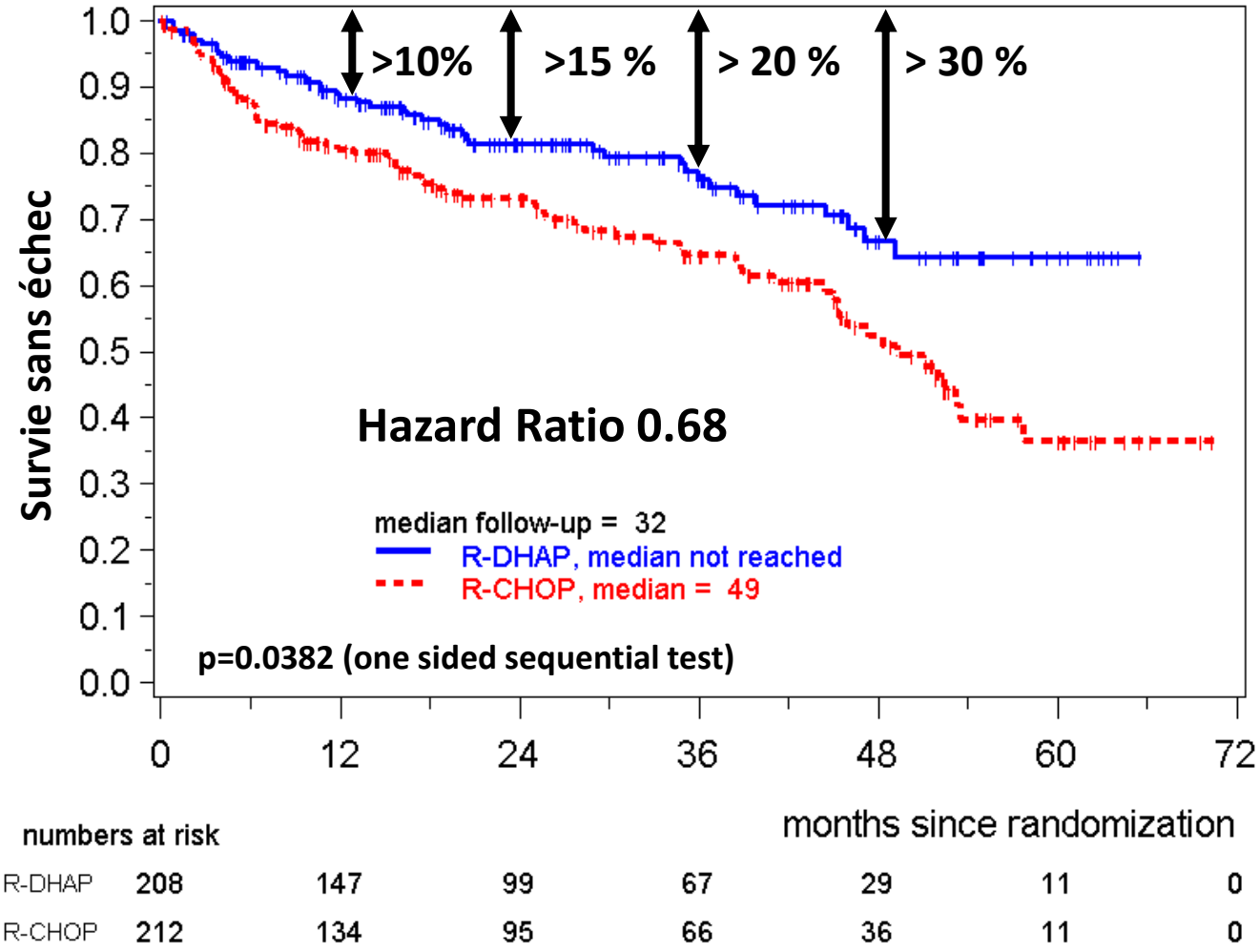


ESMO guidelines 2017

MCL patients are highly exposed to relapse

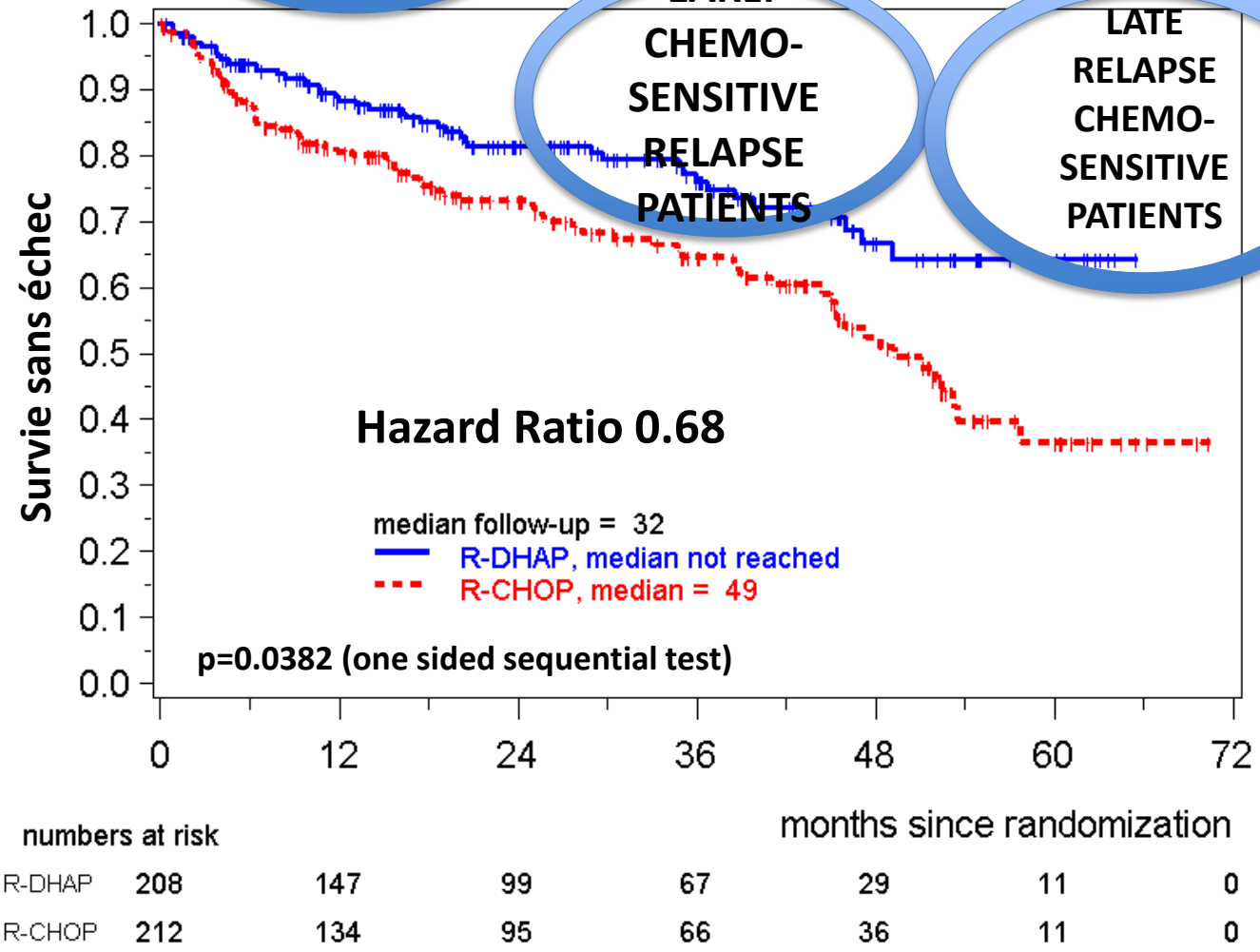


Adapté de Hermine, 2010 – Lancet 2016

PRIMARY CHEMO-REFRACTORY PATIENTS

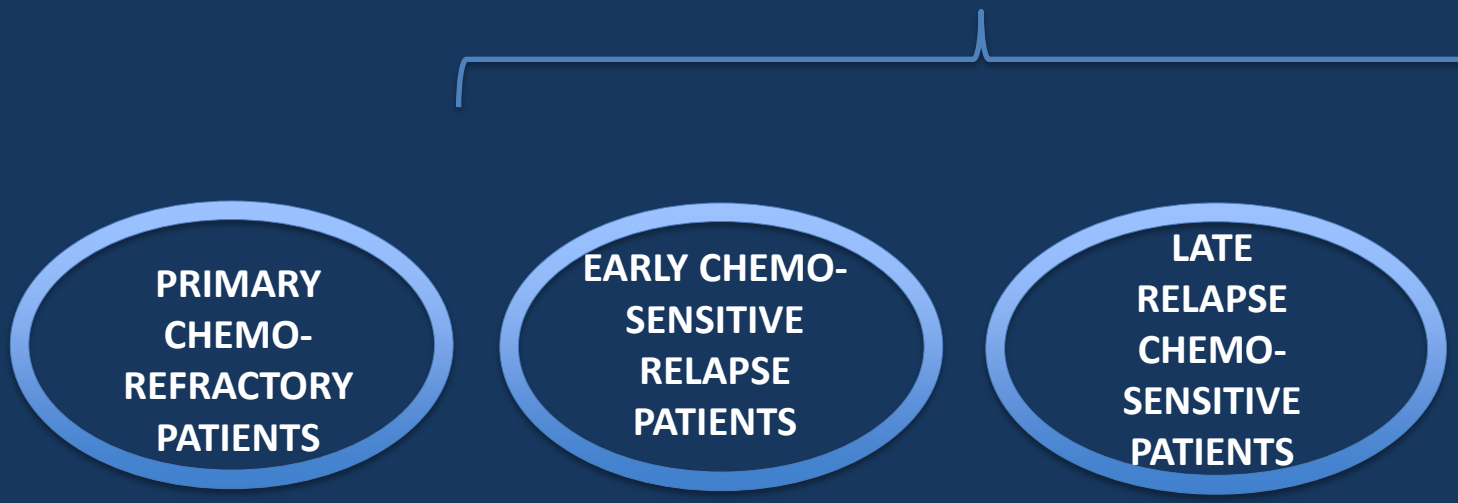
EARLY CHEMO-SENSITIVE RELAPSE PATIENTS

LATE RELAPSE CHEMO-SENSITIVE PATIENTS



Adapté de Hermine, 2010

Interest of maintenance



NEW TREATMENTS
BETTER INDUCTION

NEW TREATMENTS
BETTER INDUCTION
MAINTENANCE

NEW TREATMENTS
LESS TOXIC INDUCTION
MAINTENANCE
PRE-EMPTIVE TREATMENT
OF CLINICAL RELAPSE

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YES

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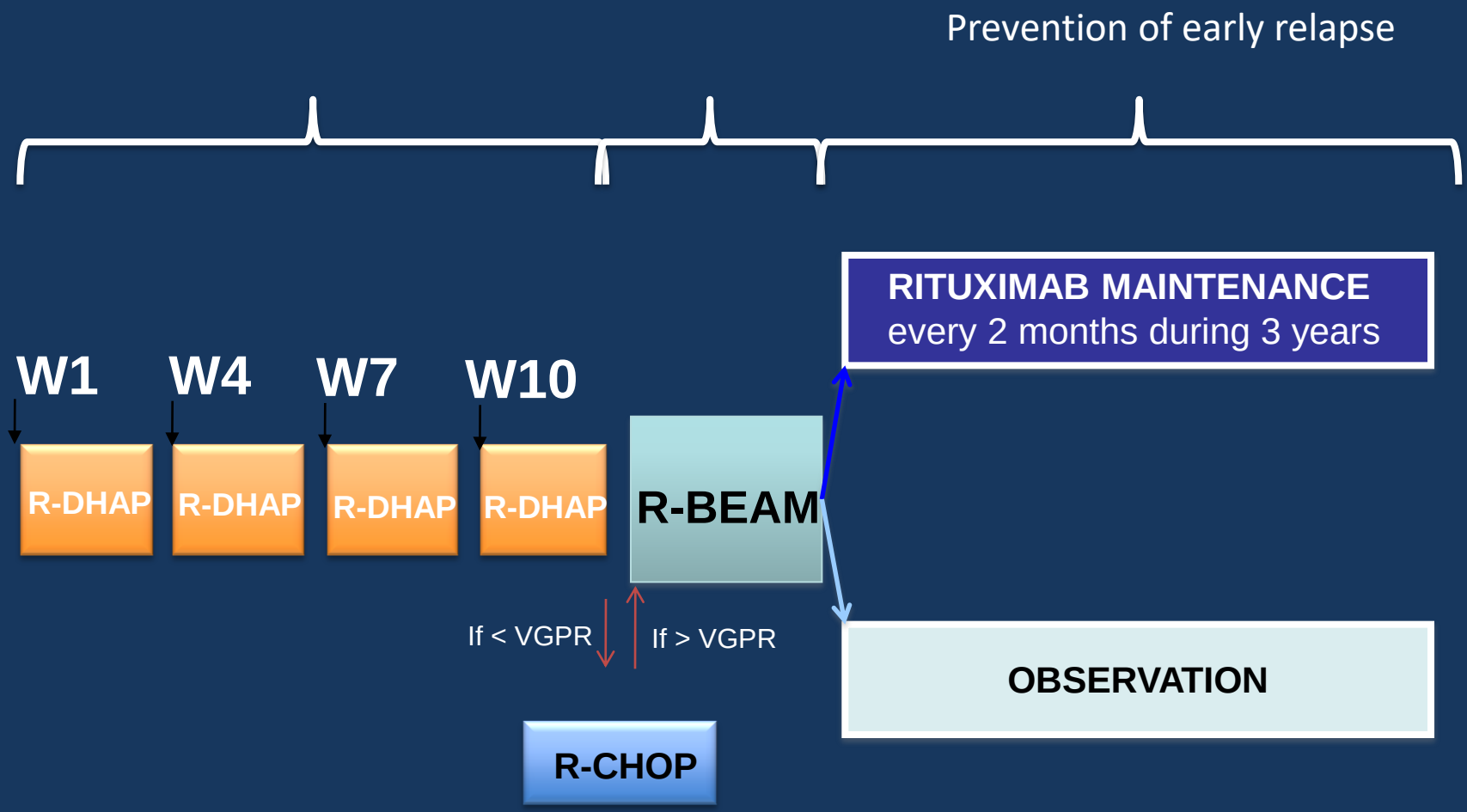
LyMa trial



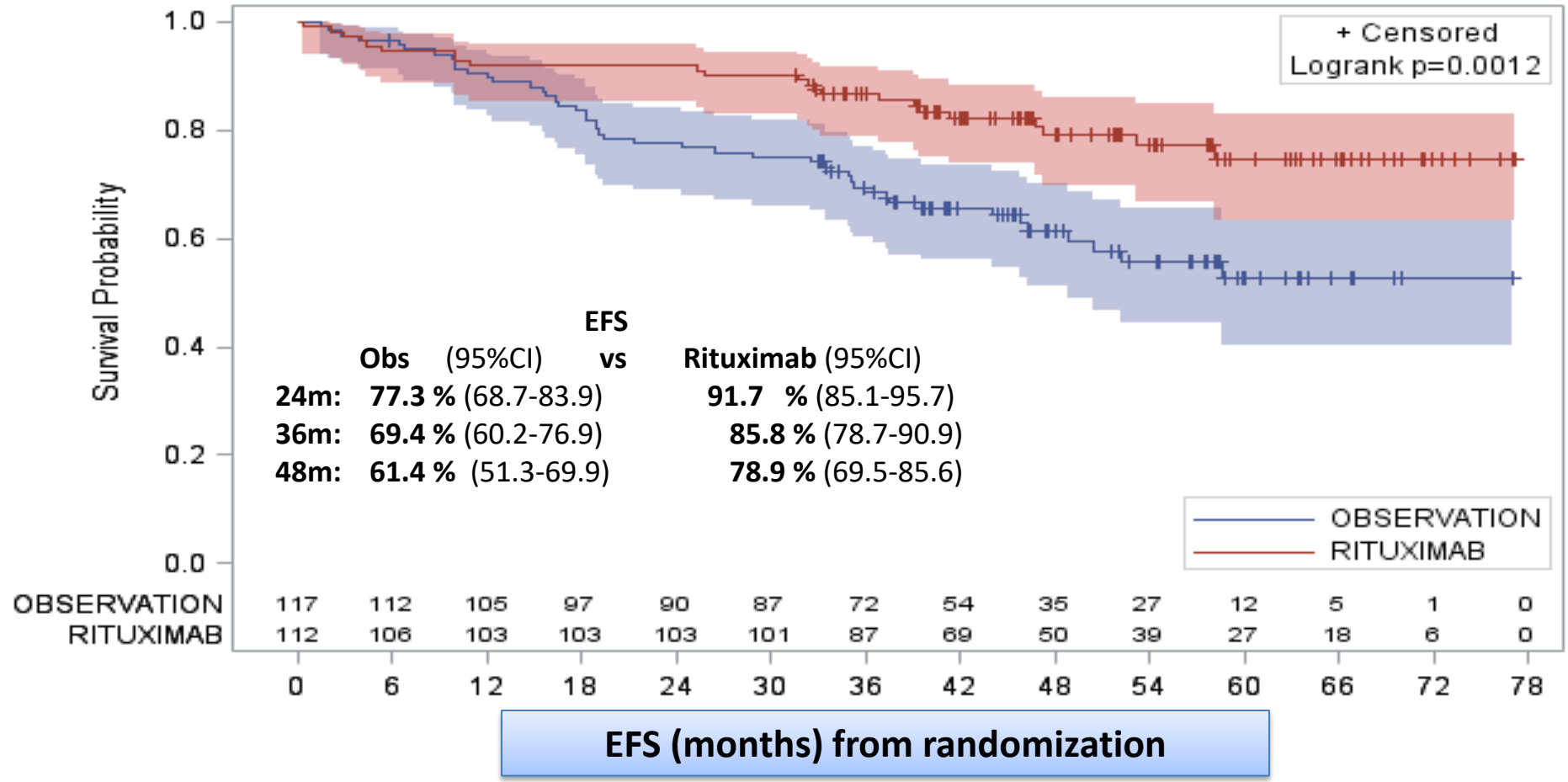
R-DHAP: Rituximab 375mg/m2; aracytine 2g/m2 x2 IV 3 hours injection 12hours interval; dexamethasone 40mg d1-4; Cisplatin 100mg/m2 d1 (or oxaliplatin or carboplatin)

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

LE GOUILL et al. ASH 2013/2014/2015/2016

EFS from Randomization

mFU: 50.2m (46.4-54.2)



PFS from Randomization

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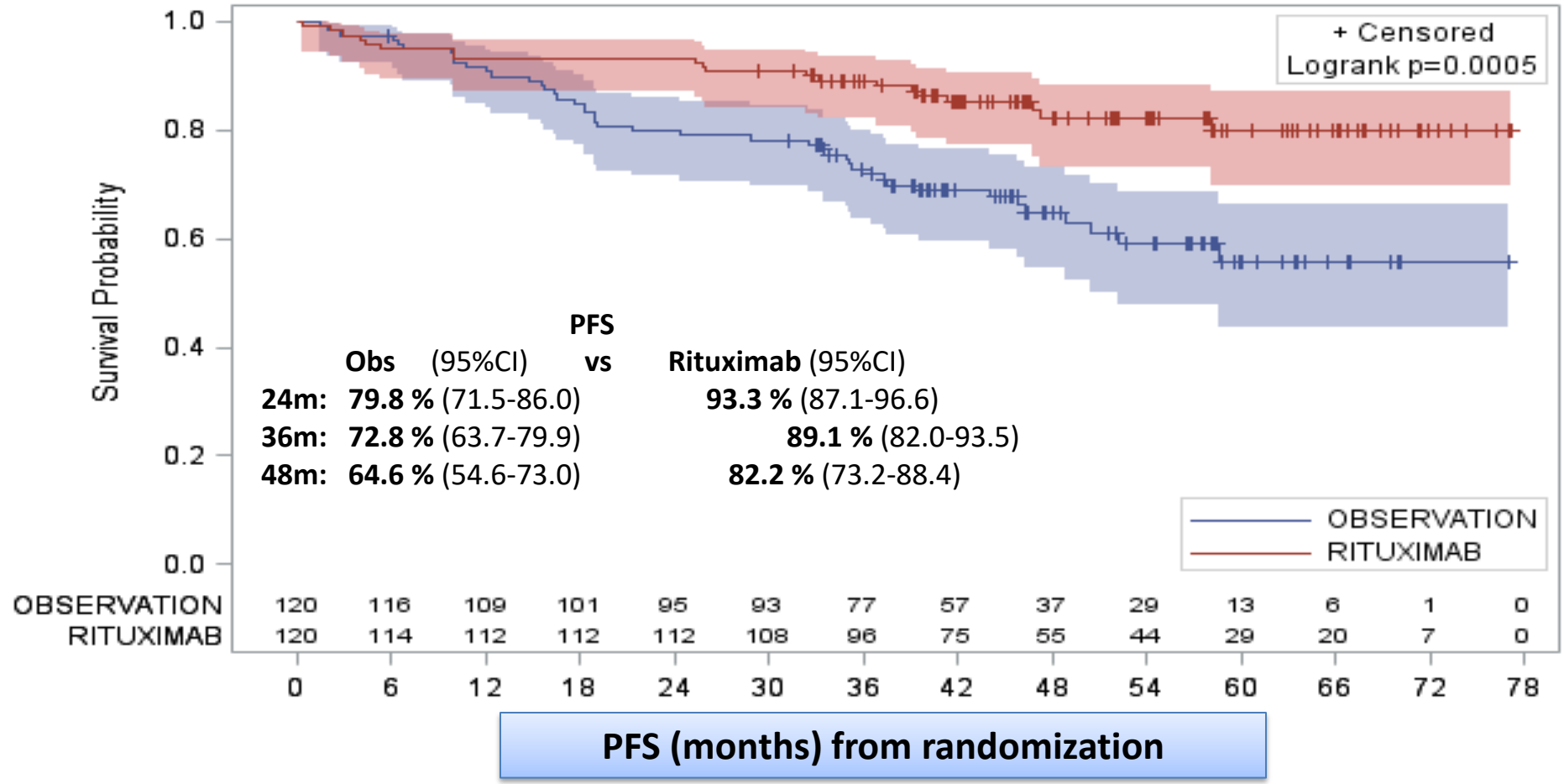
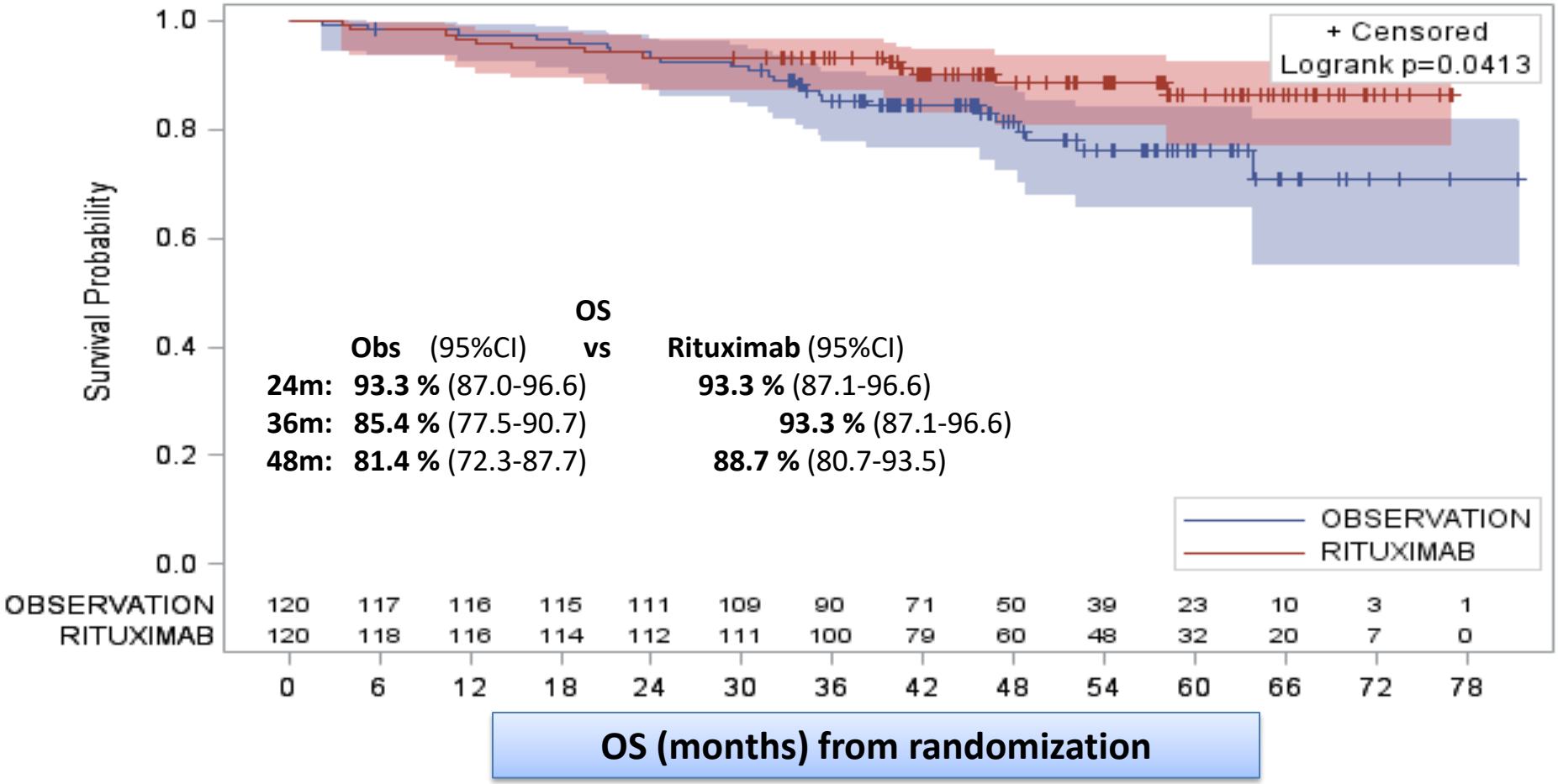


OS from Randomization

mFU: 50.2m (46.4-54.2)



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  YES it can

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- **If Yes, which drug(s) is(are) the best drug(s) for maintenance ?**

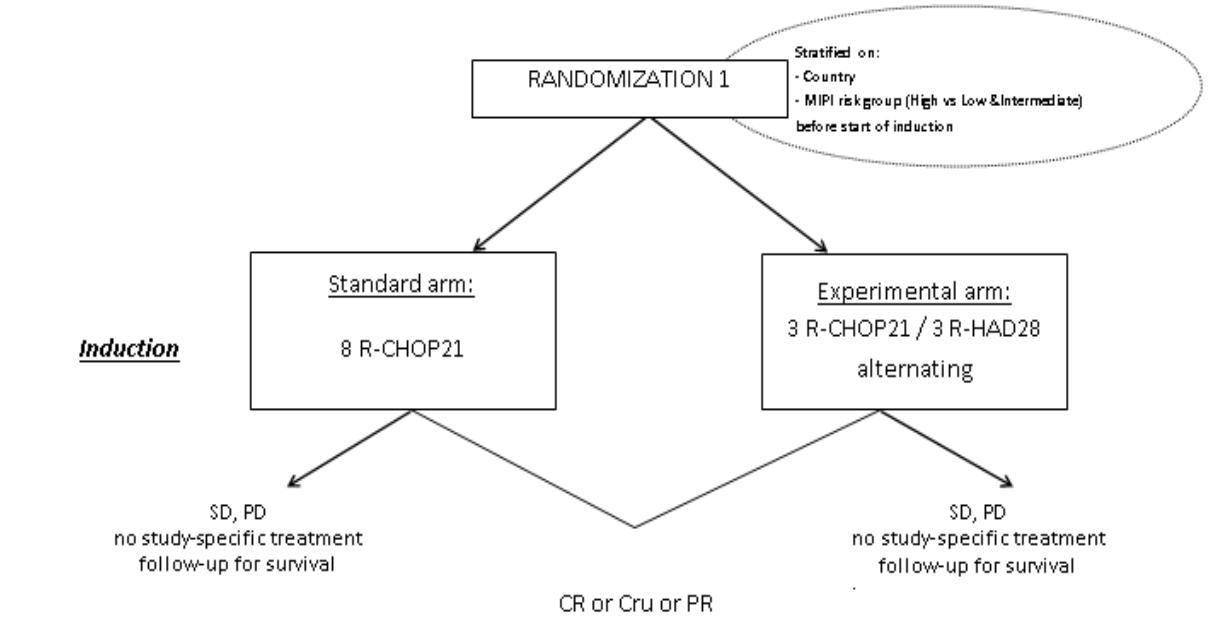
  « Rituximab Make life great again ! Rituximab maintenance is Huge ! »

  It is too simple ……
- **How long maintenance should be used ?**
- **Is there still a need for ASCT in the maintenance era ?**

Drugs that are candidate for maintenance

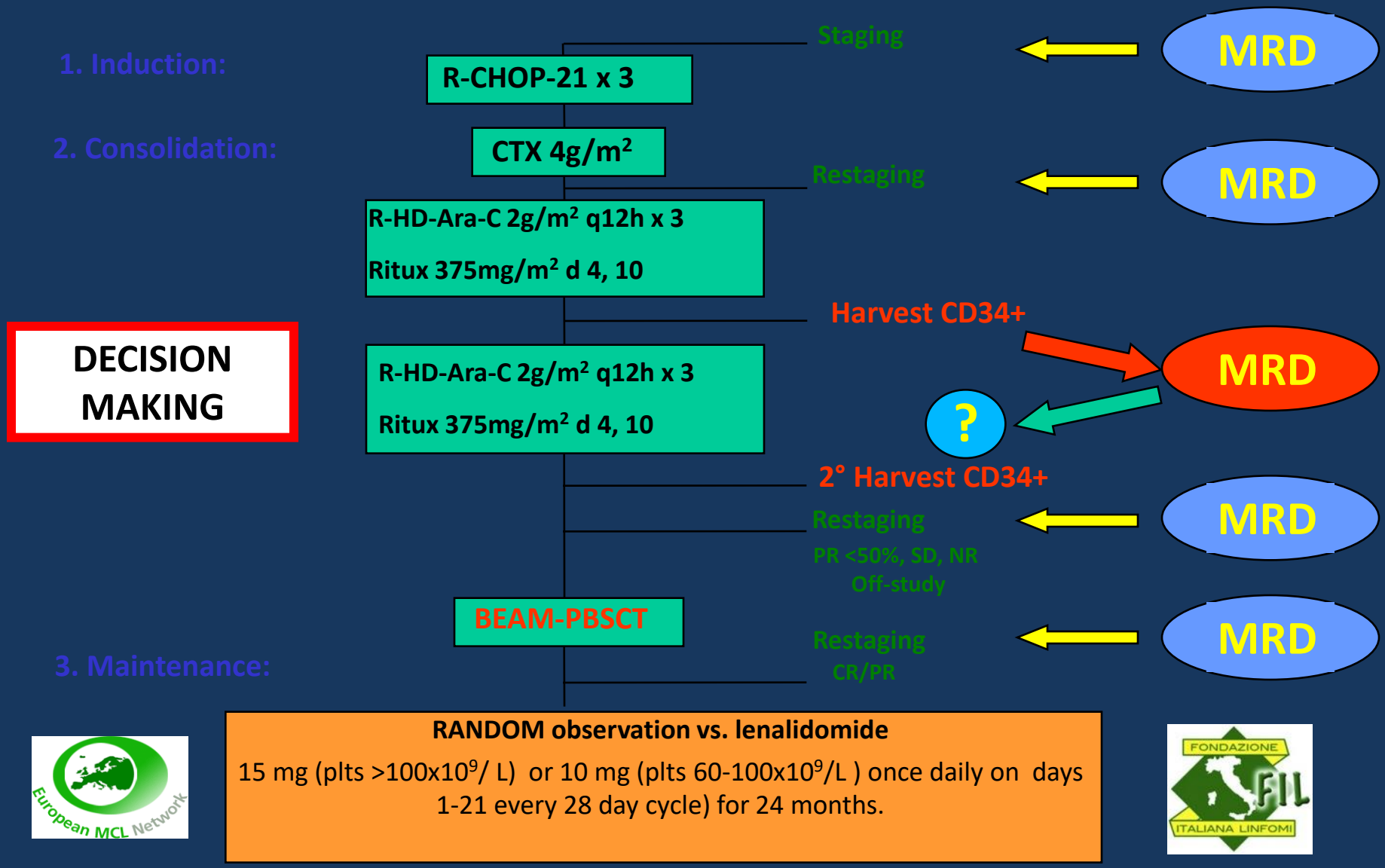
- Revlimid: oral, approved for MCL, already used for maintenance in MM, ongoing trials in MCL
- Ibrutinib: oral, approved for MCL, already used for « maintenance », ongoing trials in MCL
- ABT-199: oral, proven efficacy in MCL
- Other new BTK inhibitors, PI3K-inhibitors …

MCL-R2 elderly



MCL < 65 yrs: a new protocol for first line therapy FIL-MCL0208 (*PI Sergio Cortelazzo*)

Phase 3, 1:1 Randomized, comparative, observation-controlled study after completion of intensive immunochemotherapy followed by ASCT



MCL3002 - study design

Phase 3, randomized, double-blind, placebo-controlled study (SHINE study)

520 patients (~260 per arm)

Randomization

Arm A[a]

Background therapy (6 cycles):
Bendamustine (90 mg/m^2 IV Days 1-2)
Rituximab (375 mg/m^2 Day 1)

CR/PR →
Rituximab 375 mg/m^2
(every 2 cycles, 2 years)

Study drug:
Oral placebo (starting on Cycle 1, Day 1)
until PD or unacceptable toxicity

Arm B[a]

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Rituximab (375 mg/m^2 Day 1)

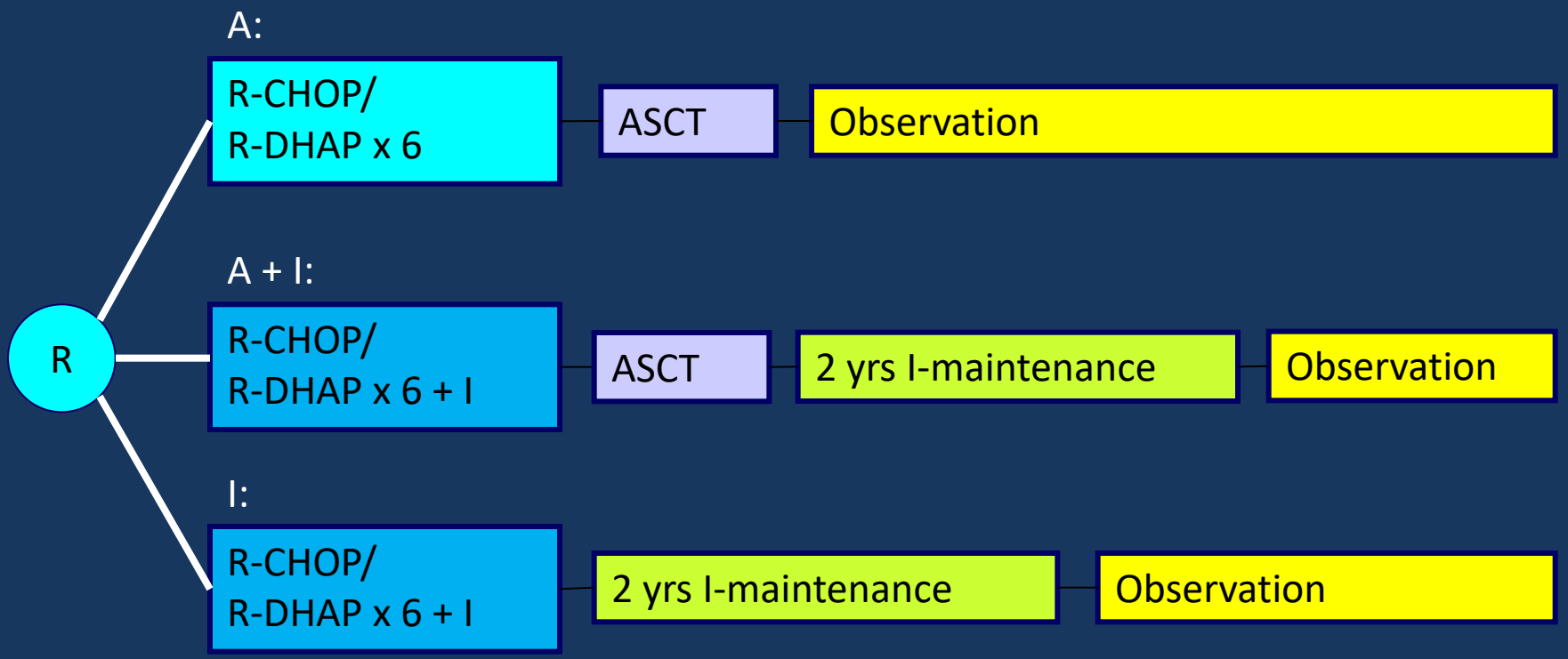
CR/PR →
Rituximab 375 mg/m^2
(every 2 cycles, 2 years)

Study drug:
Oral ibrutinib 560 mg (starting on Cycle 1, Day 1) until PD or unacceptable toxicity

[a]A cycle is defined as 28 days

Triangle

add on vs head to head comparison



superiority/non-inferiority: time to treatment failure
HR: 0.60; 65% vs. 77% vs. 49% at 5 years

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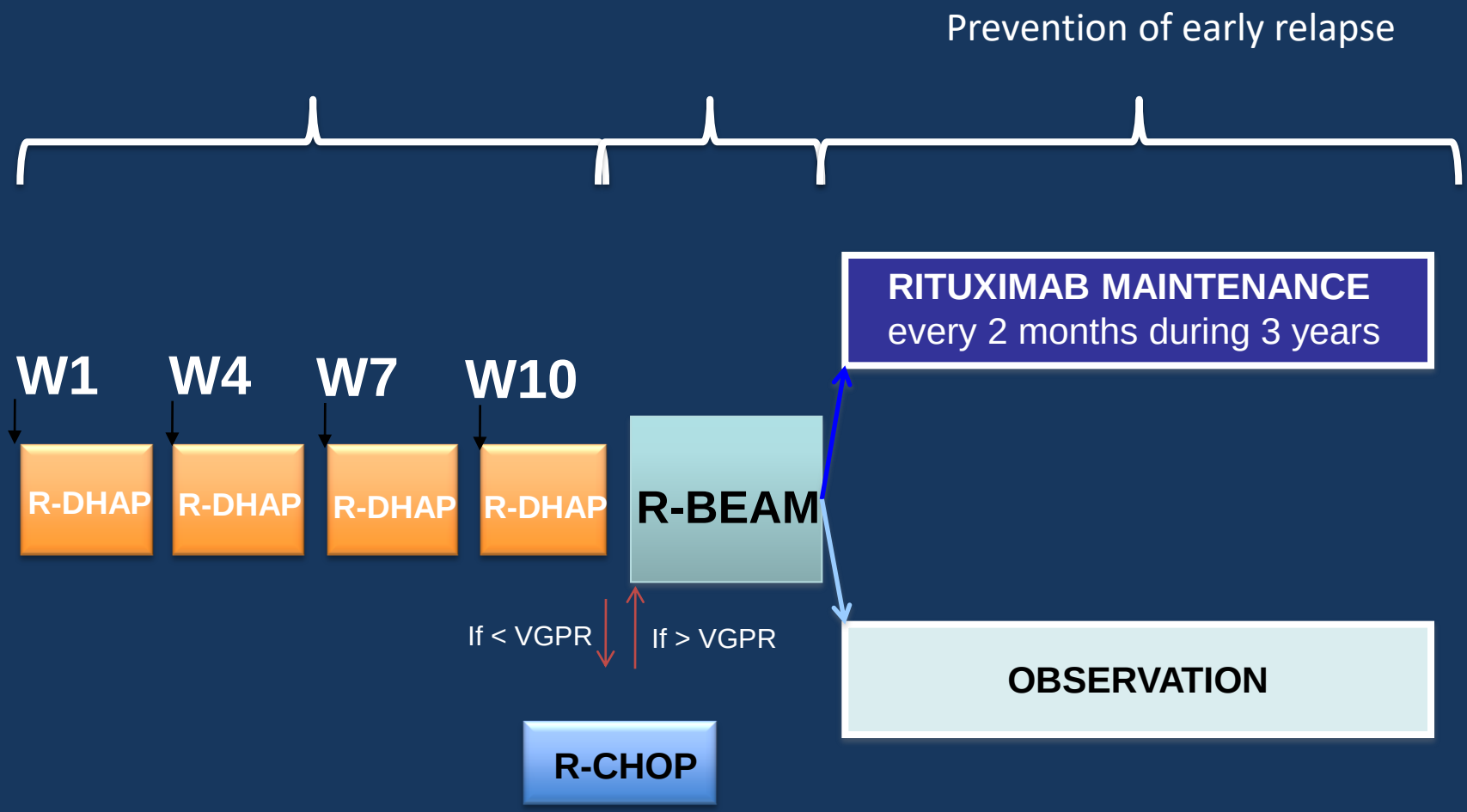

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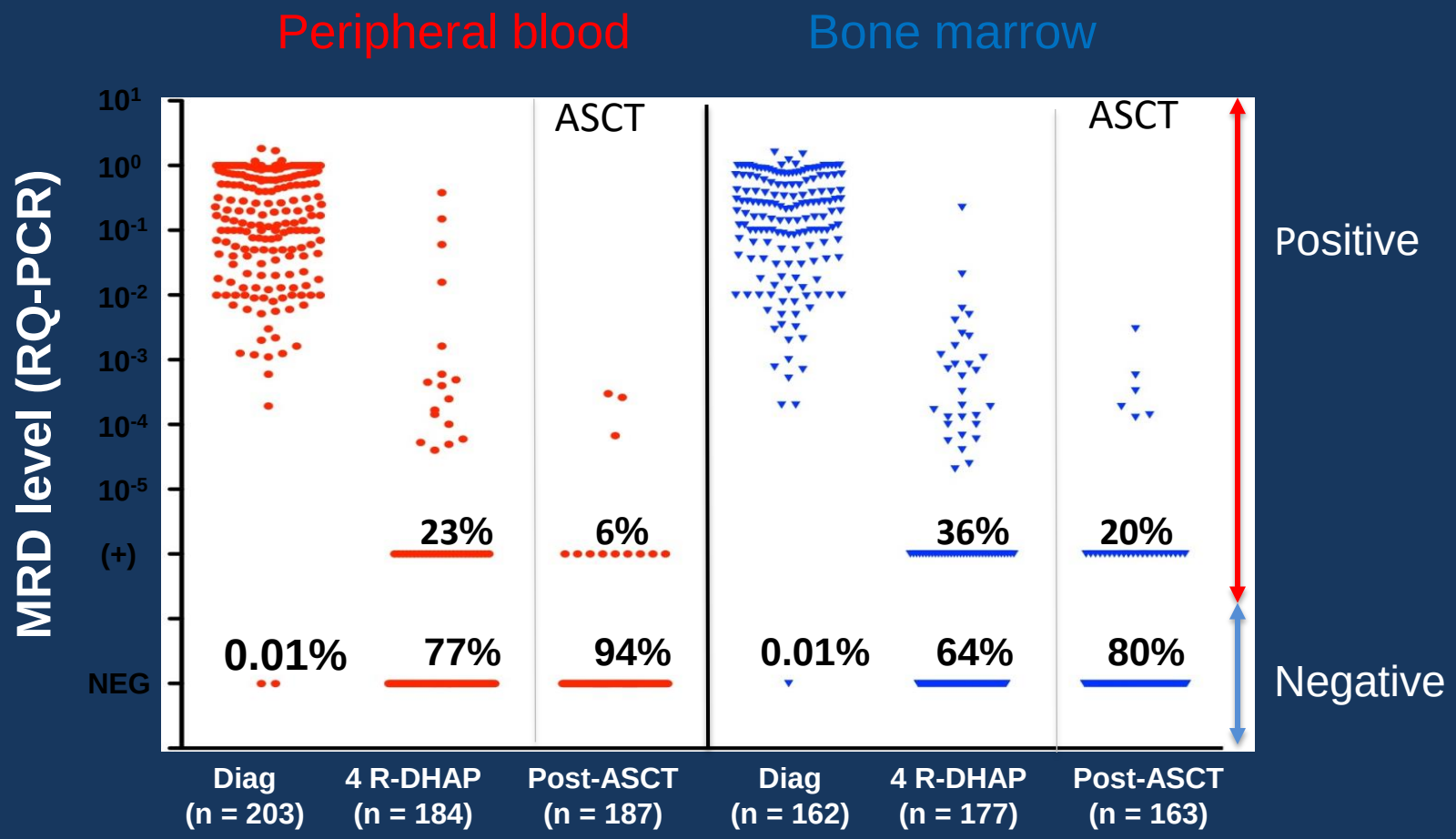
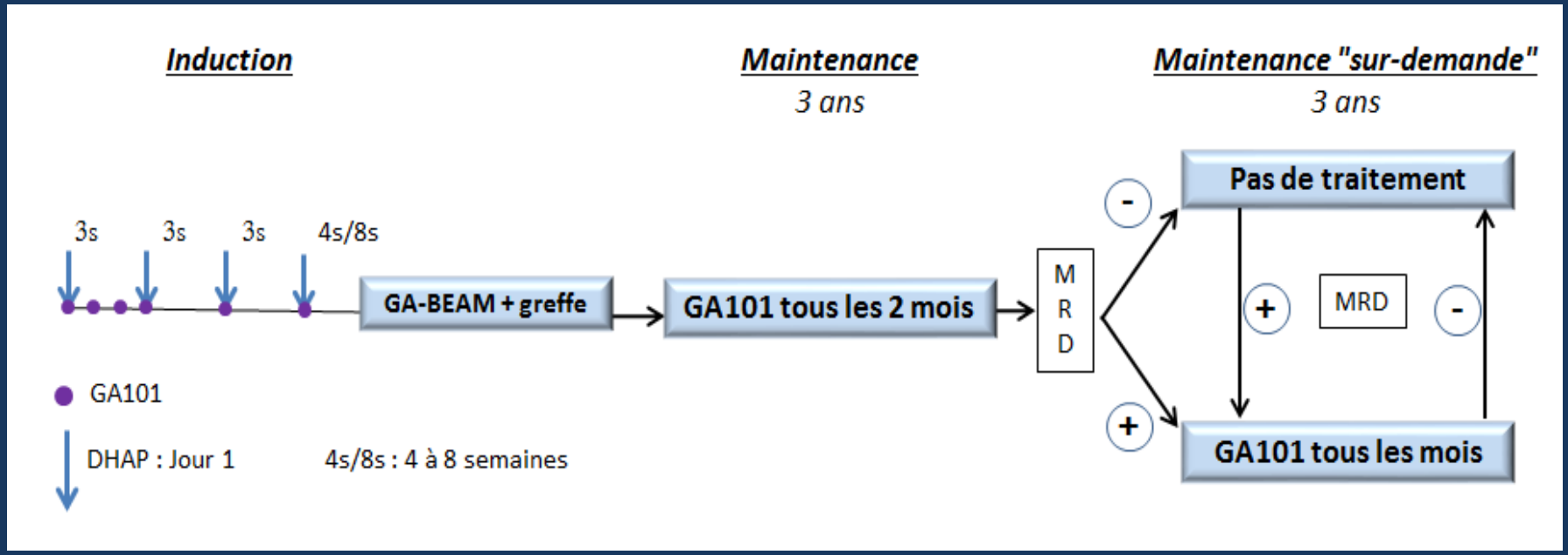
LE GOUILL et al. ASH 2013/2014/2015/2016

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



Callanan et al. Orlando, ASH 2015, Abstract 338

LYMA 101



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- At least 3 years (for all patients ?)
- **Is there still a need for ASCT in the maintenance era ?**

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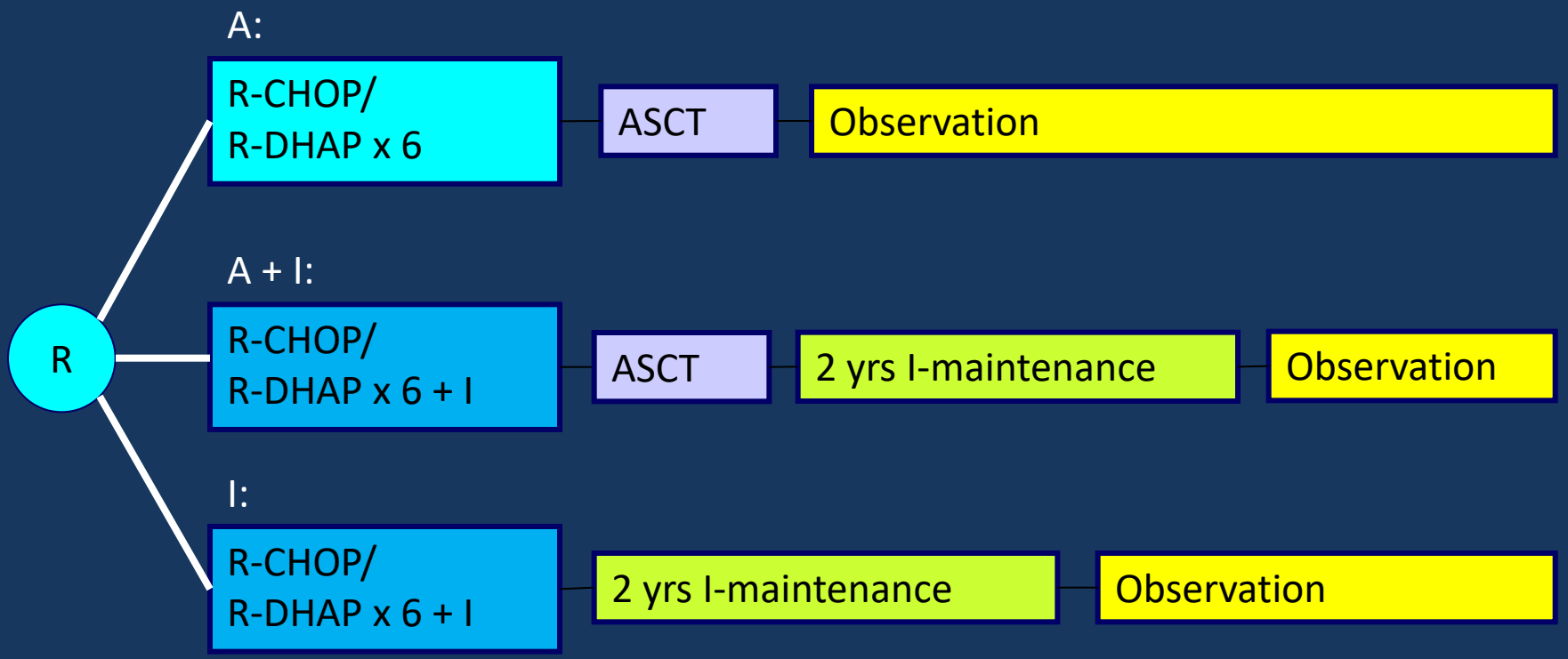

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- **How long Rituximab maintenance should be used ?**
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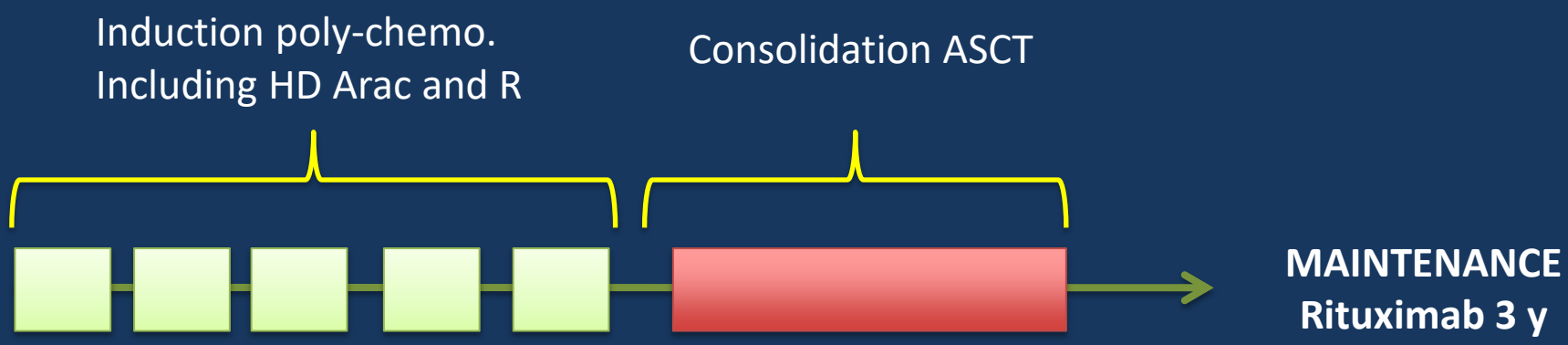
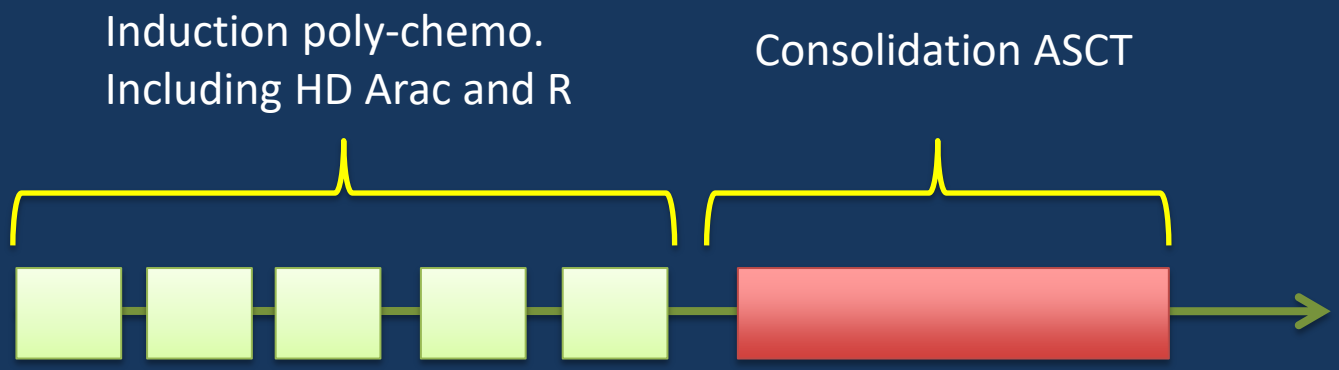
- Maybe not ….. However, today ASCT remains standard of care

Conclusion (1)

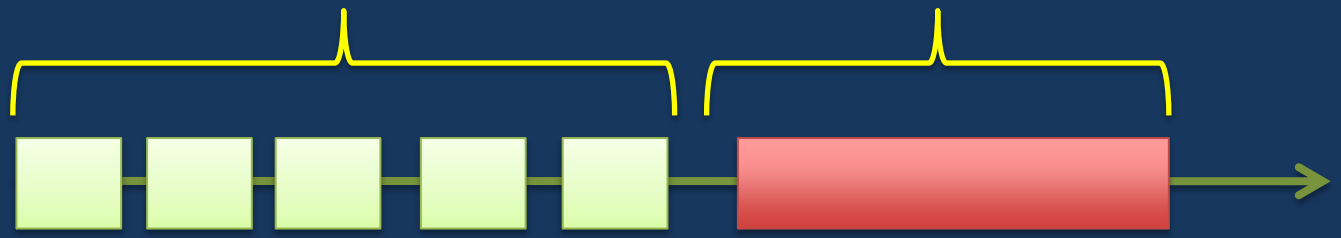


Conclusion (2)



MAINTENANCE
Rituximab 3 y
vs
Other drug + R ?
Or
New drug without R
?

Conclusion (2)



+
Other drugs ?
Or
No-chemo ?

Still needed ?
Role of MRD monitoring ?

MAINTENANCE
Rituximab 3 y
vs
Other drug(s) +R ?
Or
New drug without R ?
vs
Role of MRD monitoring ?
Duration of Maintenance ?
MRD-driven maintenance ?

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