MANTLE CELL LYMPHOMA

CLINICAL CASE PRESENTATION

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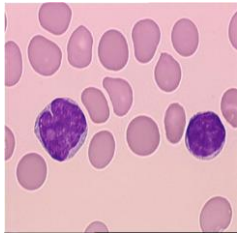
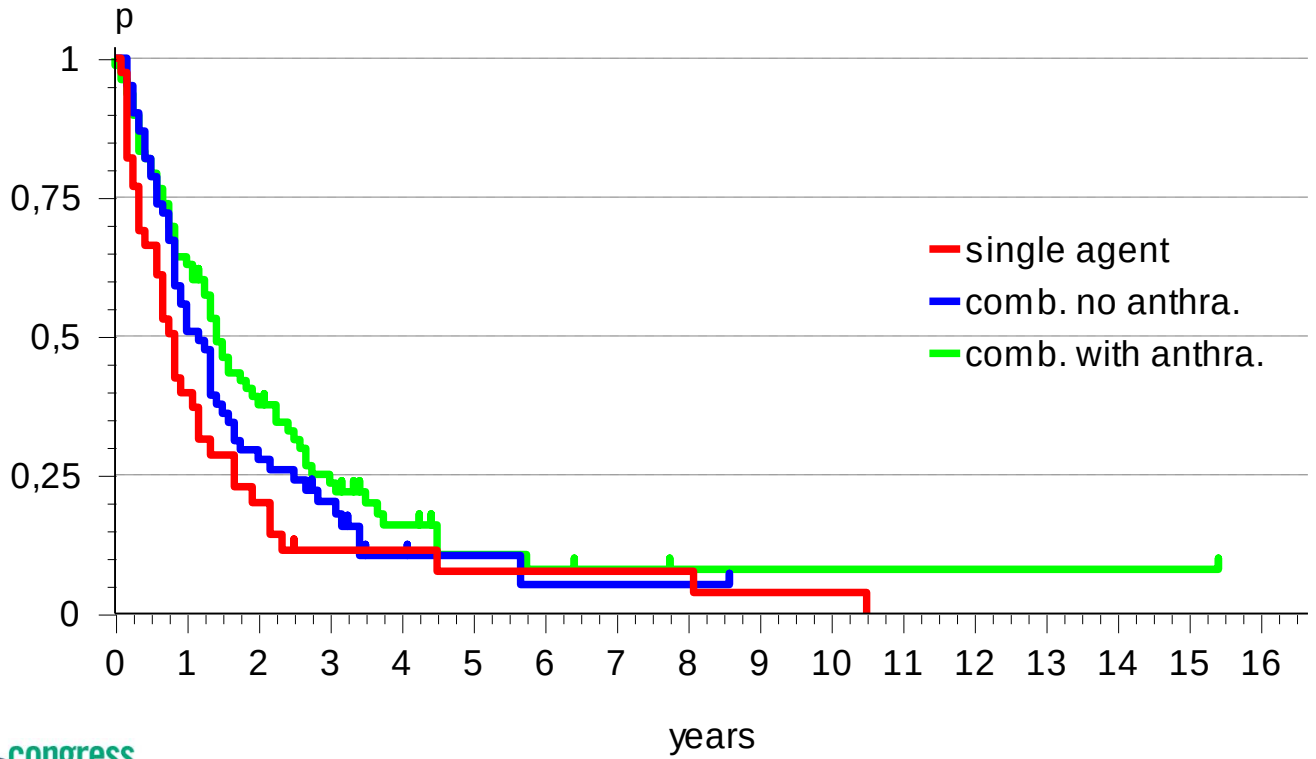


esmo.org

Multicenter Evaluation of MCL

Annency Criteria fulfilled

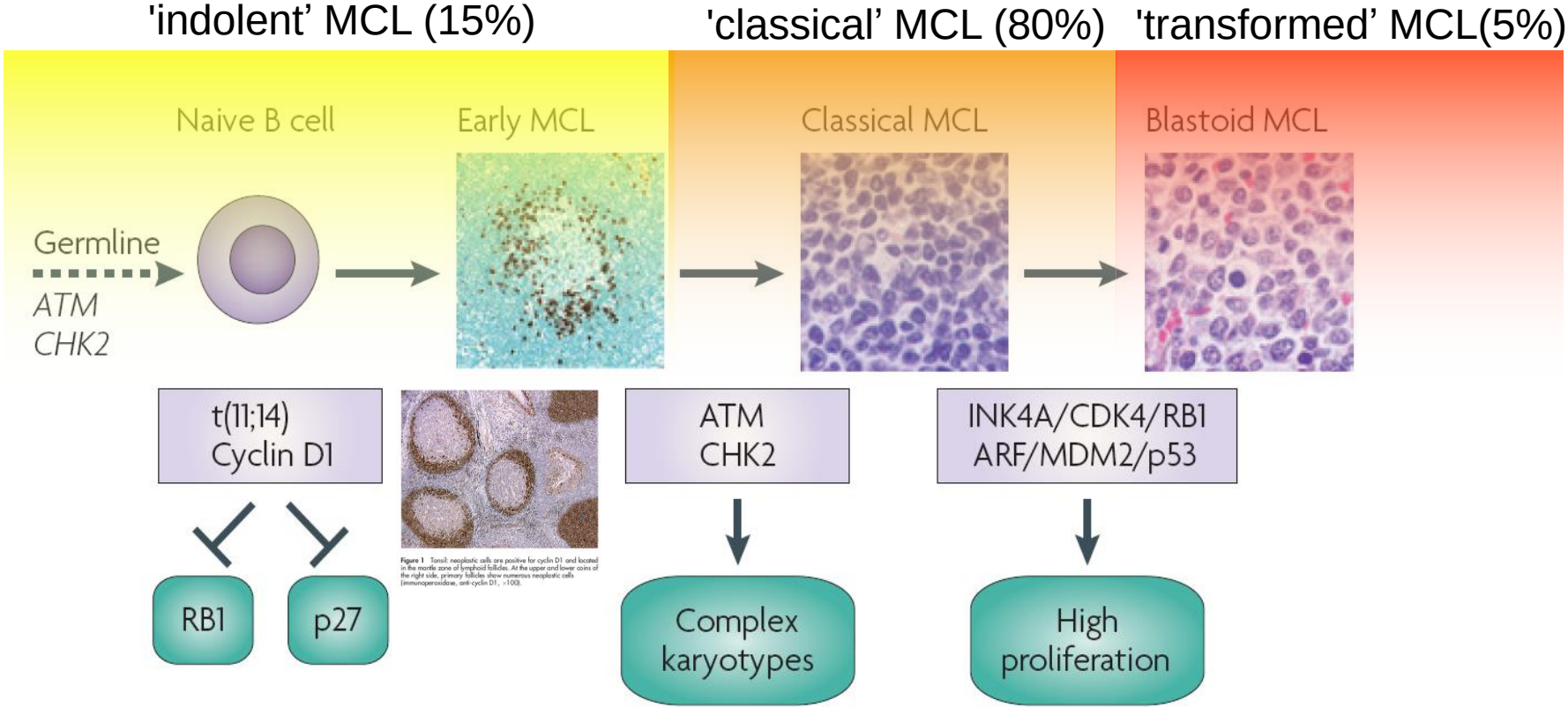
event free interval after chemotherapy in stages III + IV



anthra, anthracycline; MCL, mantle cell lymphoma

Dreyling, ASCO 1999

MCL: a spectrum of disease



MCL, mantle cell lymphoma

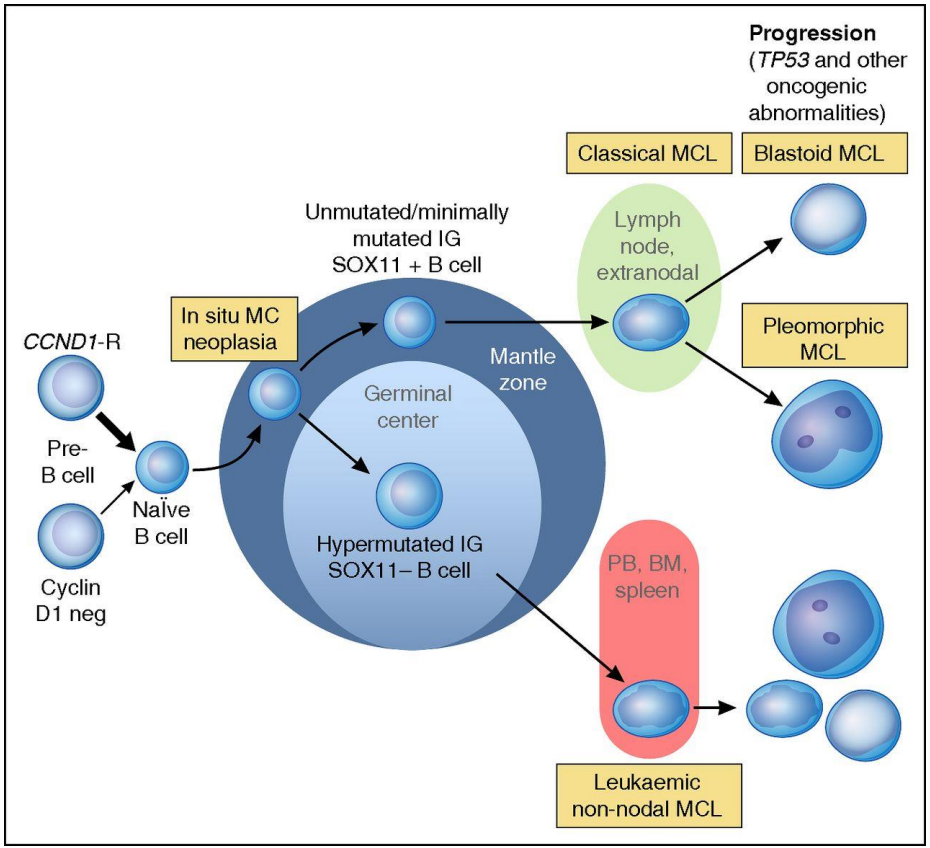
Dreyling, ESMO CR 2014

CASE 1

- Female, born 1932
- Retired textile designer, from Denmark
- Previously healthy
- 2016 lymphocytosis detected (10 x 10^9/L), normal haemoglobin and platelet count
- CT scan shows abdominal lymphadenopathy, up to 2 cm in size, spleen slightly enlarged
- Bone marrow biopsy shows 25% CD20+/CD5+/CyclinD1+ cells – mantle cell lymphoma
- No symptoms

CT, computed tomography

MCL: two kind of diseases



BM, bone marrow; IG, immunoglobulin; MC, mantle cell; MCL, mantle cell lymphoma; neg, negative; PB, peripheral blood. MCL, mantle cell lymphoma

Dreyling, ESMO CR 2017

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 28 (Supplement 4): iv62–iv71, 2017
doi:10.1093/annonc/mdx223

CLINICAL PRACTICE GUIDELINES

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

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MCL: ESMO Clinical Practice Guidelines

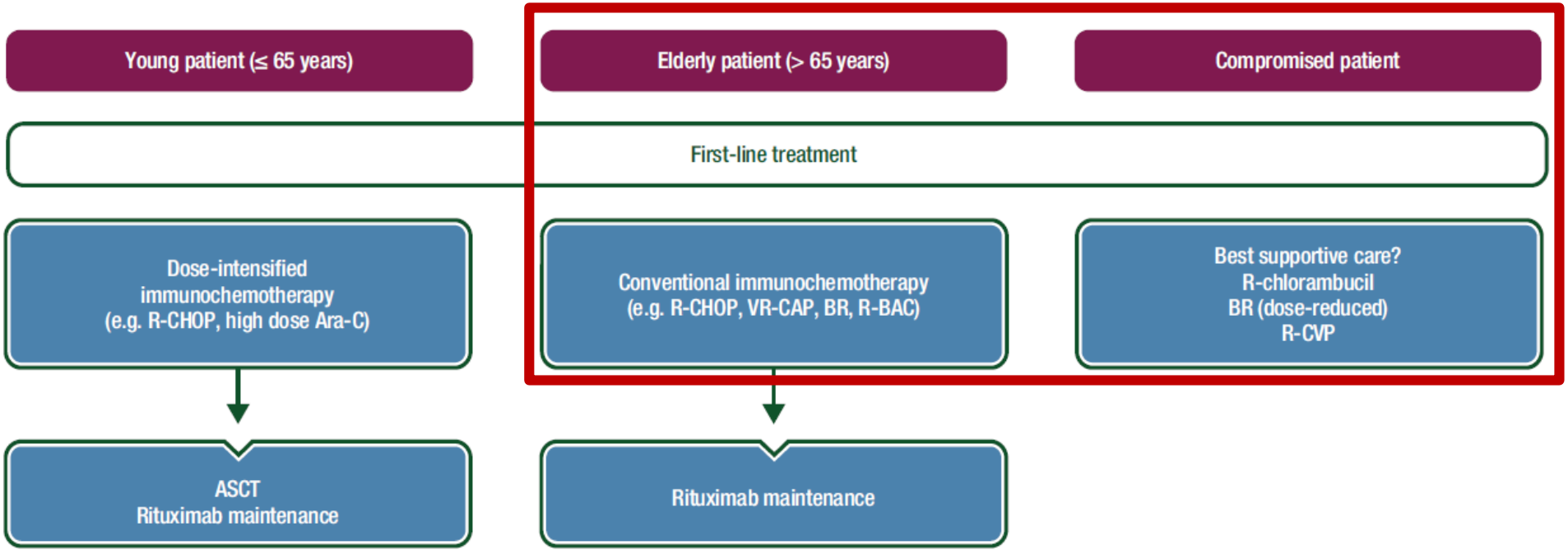
Leukaemic non-nodal subtype of MCL

However, a subset of patients may exhibit a more indolent evolution. Most of these cases are commonly characterised by a leukaemic non-nodal presentation with BM involvement only and splenomegaly [1, 8]. SOX11 negativity may help to identify these cases. In addition, conventional MCL (SOX11-positive) with low Ki-67 ($\leq$ 10%) tend to have a more indolent course.

Unfortunately, there are no markers that definitely predict indolent behaviour, but a short course of 'watch and wait' period under close observation seems to be appropriate in suspected indolent cases with low tumour burden [III, B] [10].

Dreyling, ESMO CR 2017

MCL: ESMO Clinical Practice Guidelines



ASCT, autologous stem cell transplantation; BAC, bendamustine and cytarabine; BR, bendamustine and rituximab; Ara-C, cytarabine; CHOP, cyclophosphamide, doxorubicin, vincristine and prednisone; CVP, cyclophosphamide, vincristine and prednisone; R, rituximab; VR-CAP, rituximab, cyclophosphamide, doxorubicin and prednisone with bortezomib.

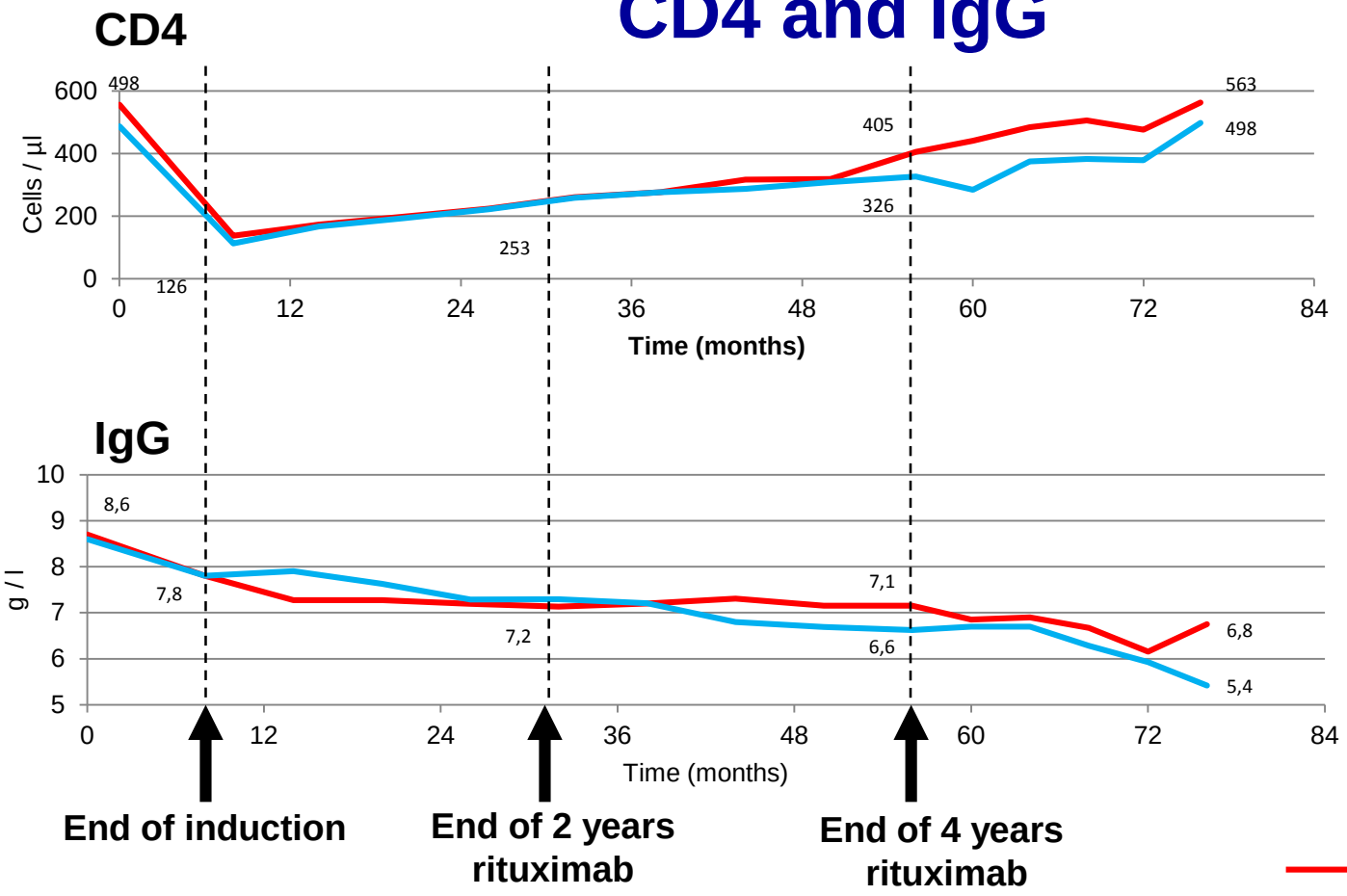
Dreyling, ESMO CR 2017

CASE 1

Female, born 1932

- In February 2018, she is started on R-bendamustine. Bendamustine dose reduced to 50% (1 day only). 6 cycles are planned
- After 2 cycles, she is hospitalised due to dyspnoea and fever, and diagnosed with a pneumocystis pneumonia. Treated with cotrimoxazole, and discharged after 10 days
- After 4 cycles, she asked to stop due to worsening fatigue. By then, lymphocytosis is normalised, no remaining lymphadenopathy or splenomegaly
- No maintenance rituximab is planned
- In August 2018, two months after stopping treatment, the patient feels well

CD4 and IgG



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Rummel, ASH 2017: #483

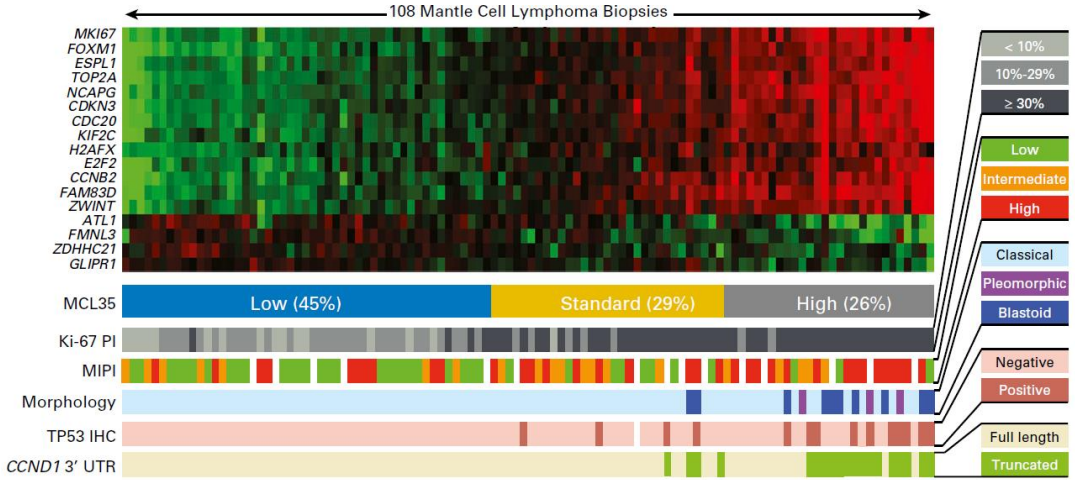
CASE 2

- Man born 1953
- Social worker
- Previously diagnosed with mitral insufficiency and impaired hearing

- November 2016 – admitted at local hospital with suspected acute lymphocytic leukemia (ALL)
  - WBC 320 x 10^9/L, hepatosplenomegaly, general lymphadenopathy
  - Immunophenotyping peripheral blood: MCL, *t(11;14)*+
- Initally treated as ALL with corticosteroids, vincristine, cyclophosphamide, but WBC -> 450
- Blood sample analysed for *TP53* mutation - positive

MCL, mantle cell lymphoma; WBC, white blood cell

Risk factor proliferation: MCL 35



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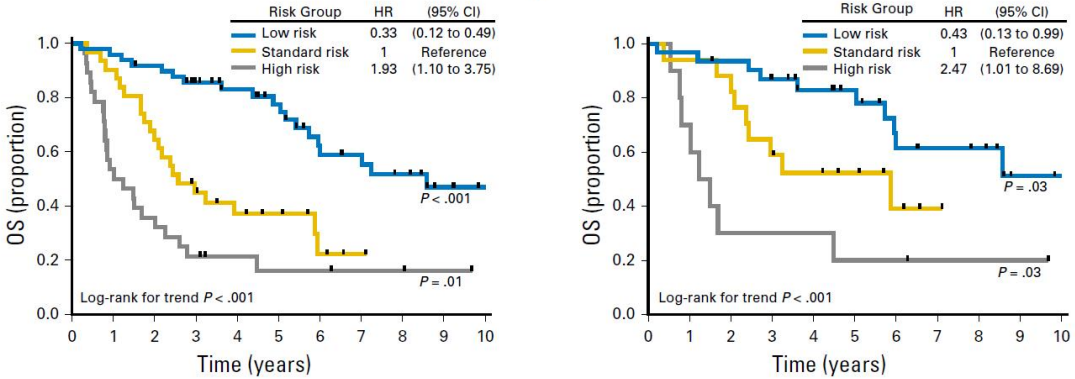

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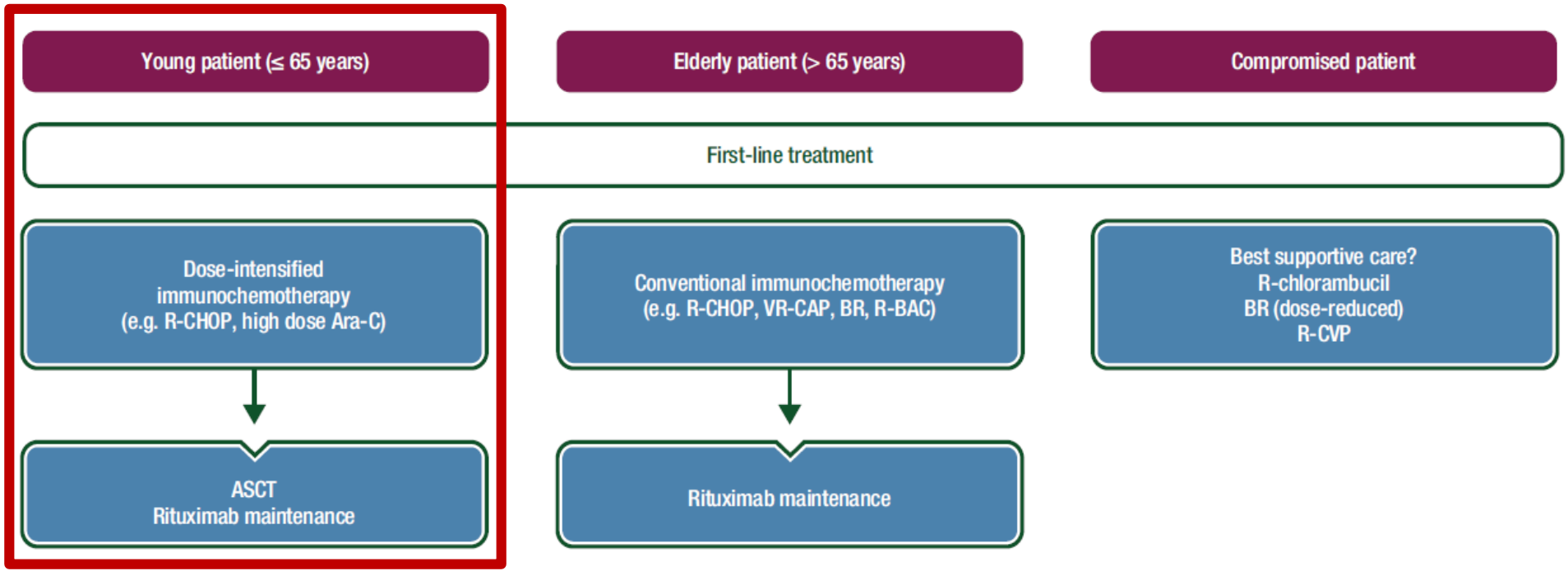
Scott, JCO 2017

MCL: ESMO Clinical Practice Guidelines



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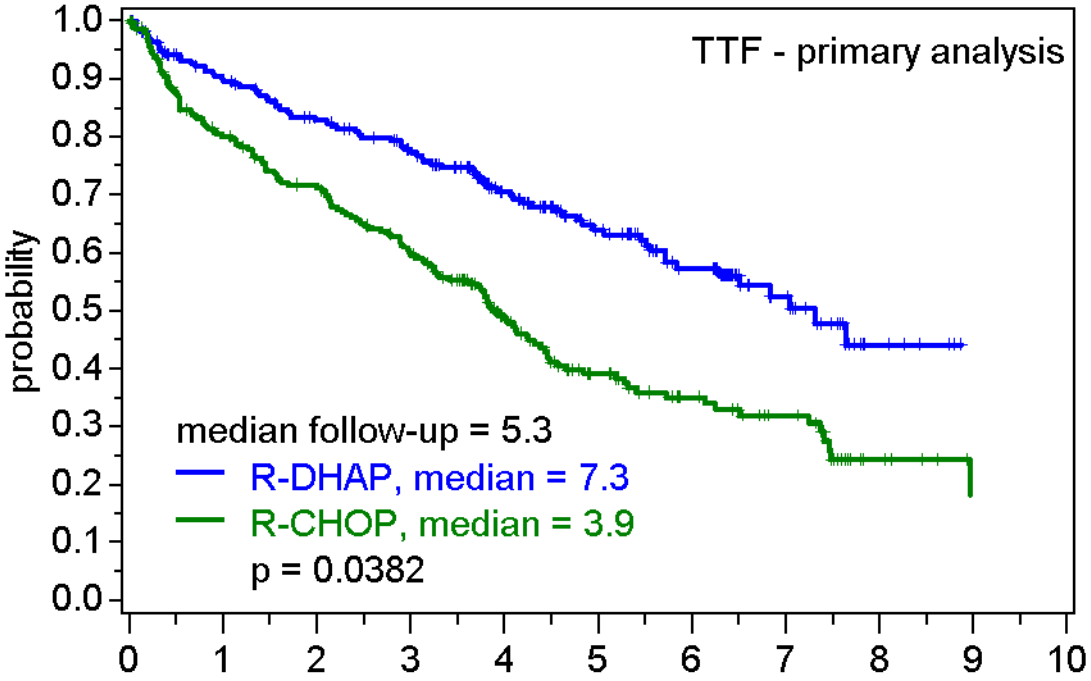
Dreyling, ESMO CR 2017

MCL younger
Time to treatment failure



Numbers At Risk

R-DHAP	232	190	170	150	111	77	52	26	6	0
R-CHOP	234	176	153	125	82	53	35	24	6	0

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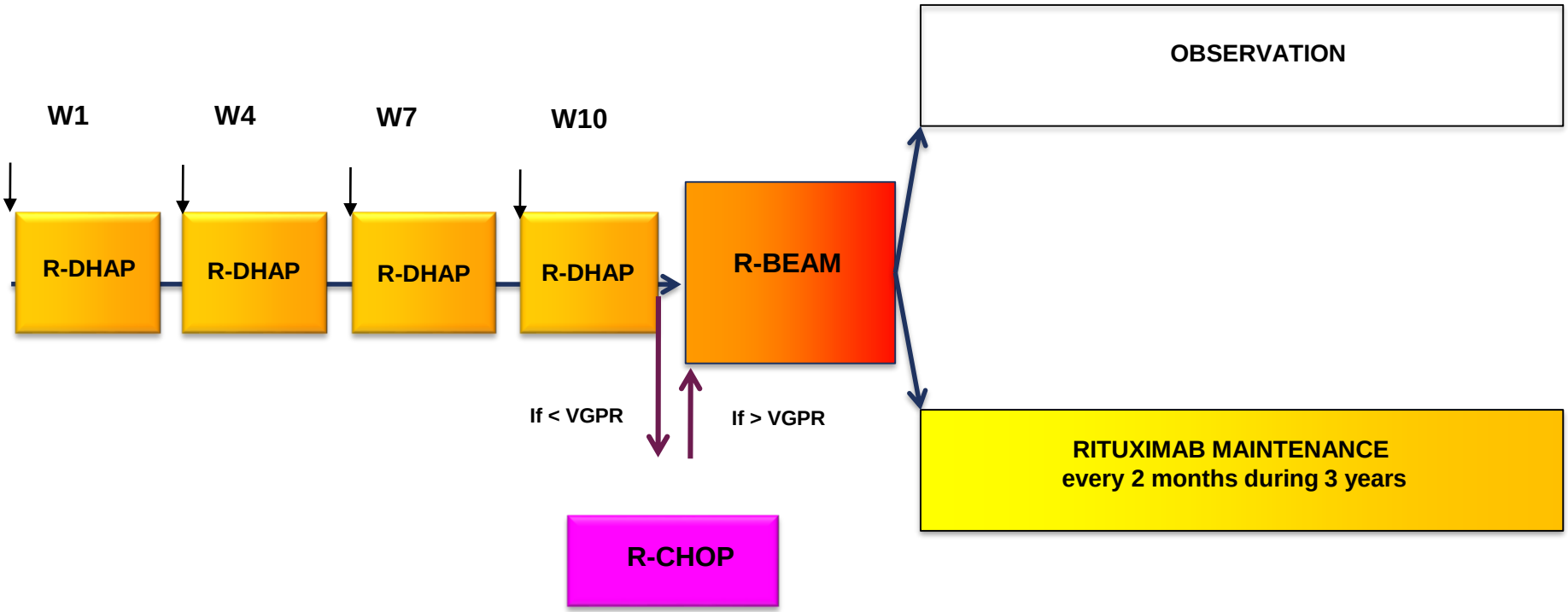
Hermine, Lancet 2016

LyMa trial



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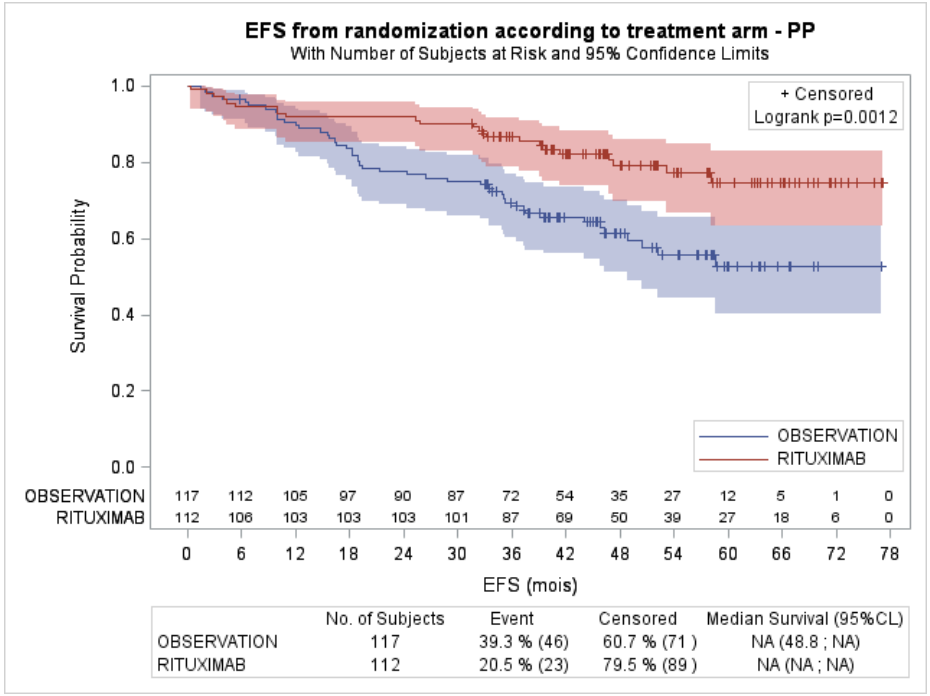
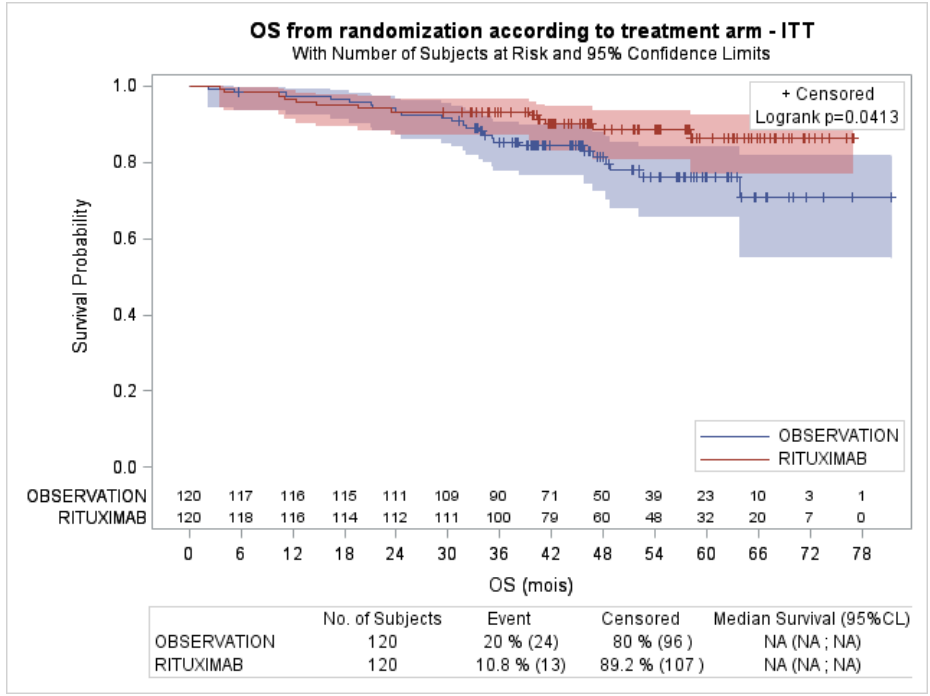
Le Gouill, NEJM 2017

Survival rates from randomisation





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Le Gouill, NEJM 2017

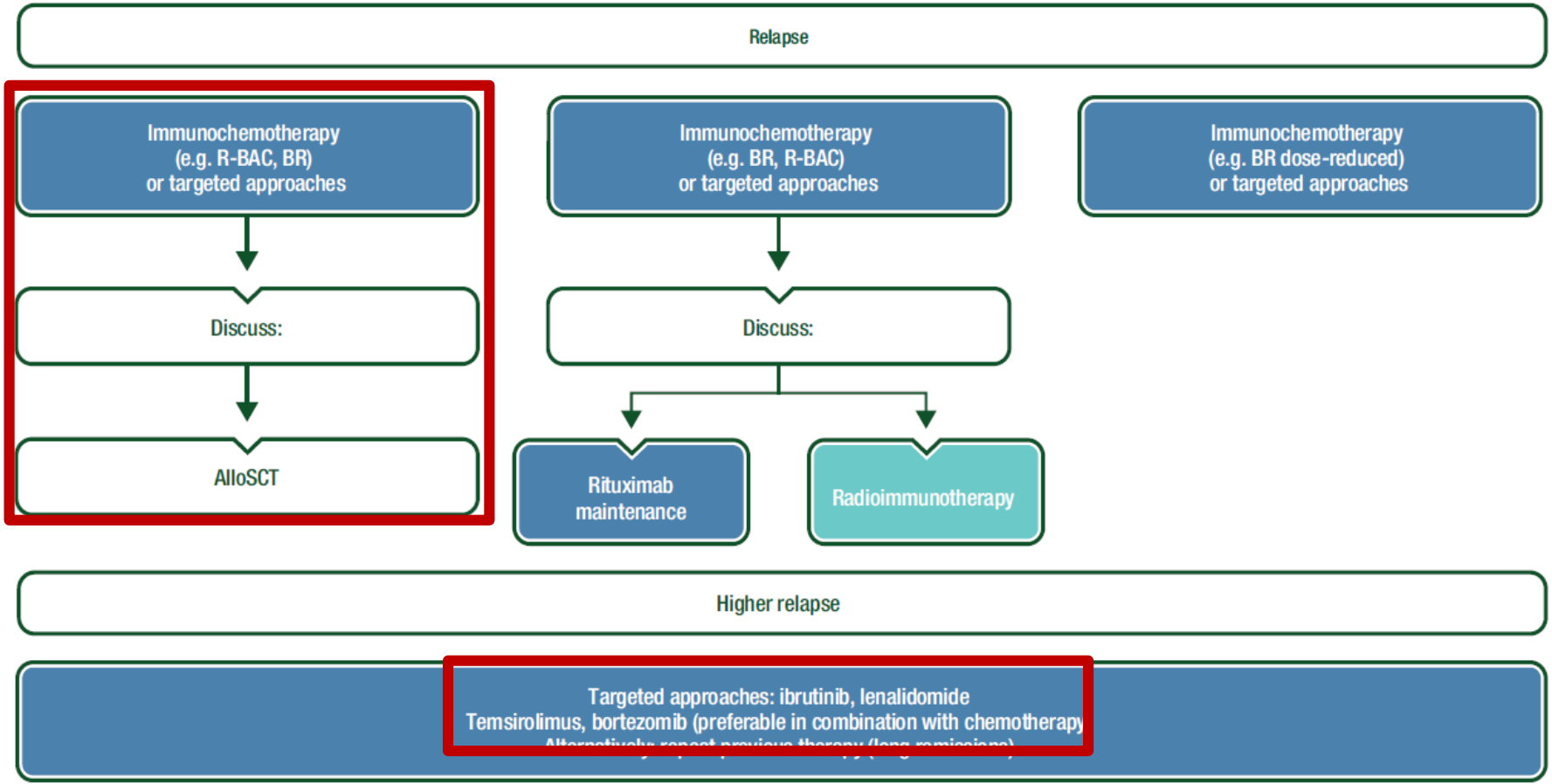
CASE 2

- Man born 1953
- Received high dose cytarabine as in Nordic MCL2 – only transient response
- Started on rituximab + ibrutinib 560 mg/day
- March 2017 – CR. Unrelated donor identified. Allo-SCT planned ASAP. Patient hesitant – prefers to wait until after summer

- August 2017 - minimal bone marrow involvement
- September 2017 – bulky abdominal mass
- Ibrutinib resistance – stopped, started on R-bendamustine
- After 2 weeks rapid progression – bilateral hydronephrosis – dies Oct 2017 due to progressive MCL

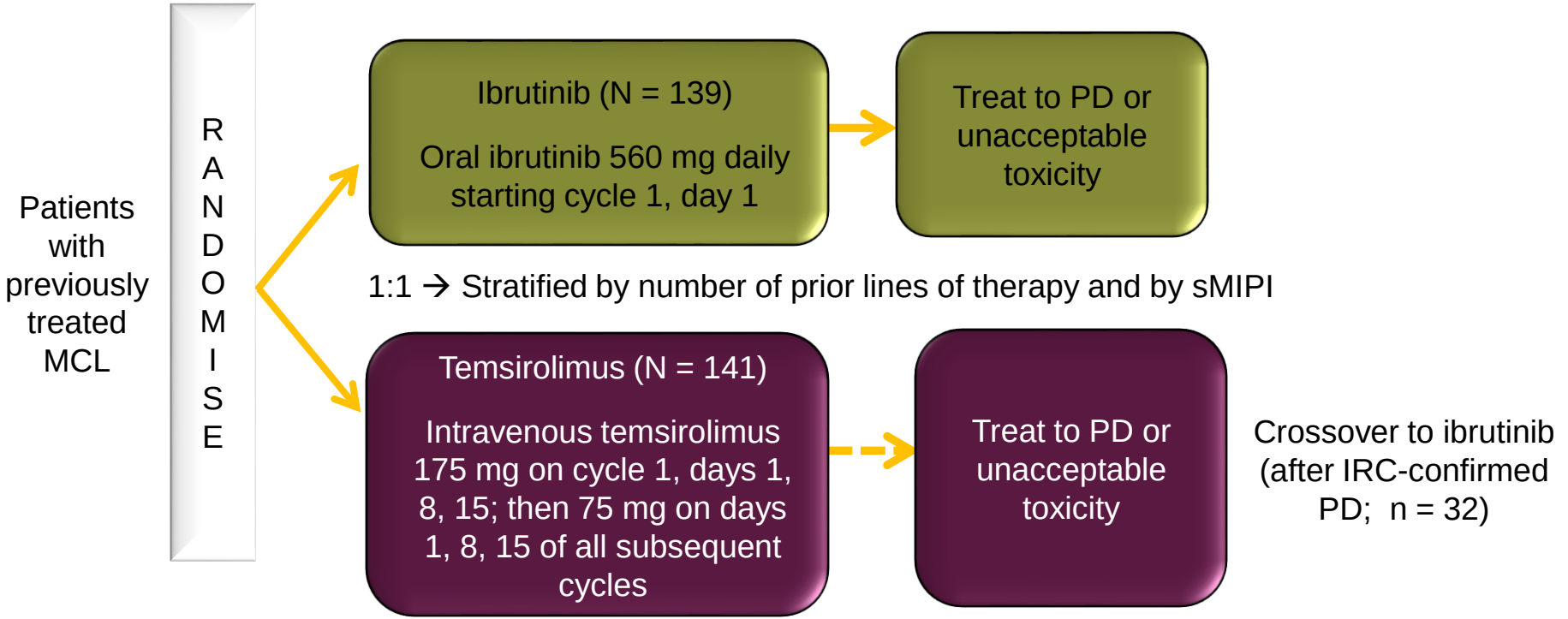
Allo-SCT, allogeneic hematopoietic stem cell transplantation; MCL, mantle cell lymphoma

MCL: ESMO Clinical Practice Guidelines



Dreyling, ESMO CR 2017

MCL3001 (RAY): Phase 3 Study



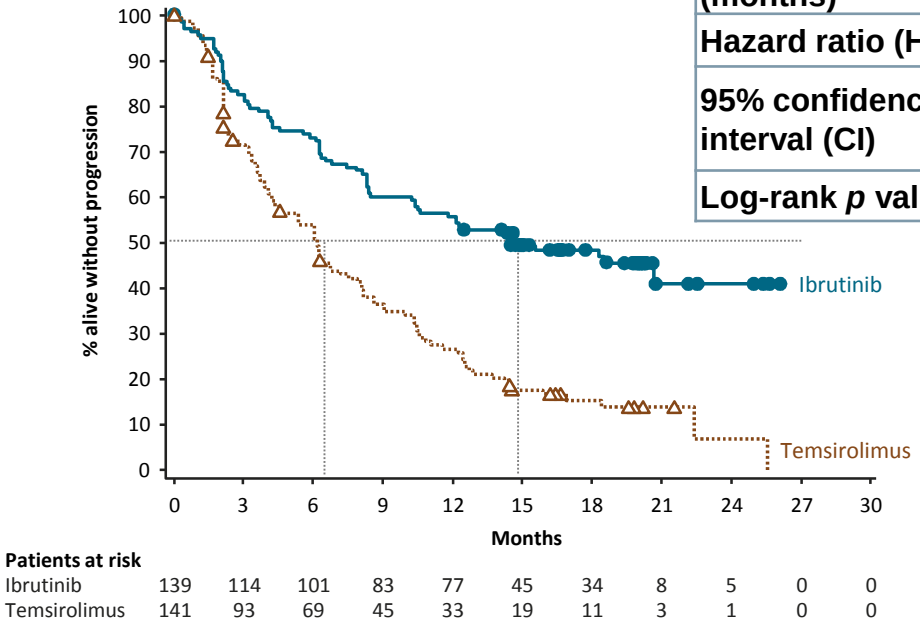
MCL, mantle cell lymphoma; PD, progressive disease; WBC, white blood cell

Dreyling, Lancet 2015

Progression-free survival (PFS)

ITT population
Median follow-up: 20 months

	Ibrutinib	Temsirolimus
Median PFS (months)	14.6	6.2
Hazard ratio (HR)	0.43	
95% confidence interval (CI)	0.32-0.58	
Log-rank *p* value	< 0.0001	



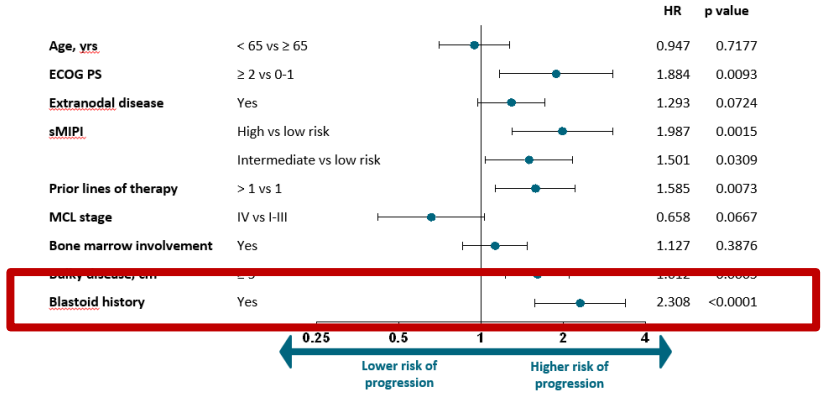
At a 2-year landmark, the PFS rate was 41% for ibrutinib versus 7% for temsirolimus

Investigator-assessed HR for ibrutinib versus temsirolimus was 0.43 (95% CI, 0.32-0.58)

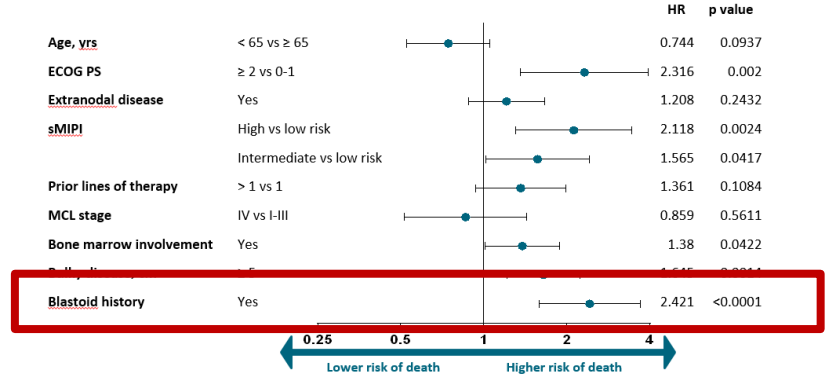
Dreyling, Lancet 2015

Independent predictors of PFS and OS with Ibrutinib: Multivariate Analysis

PFS



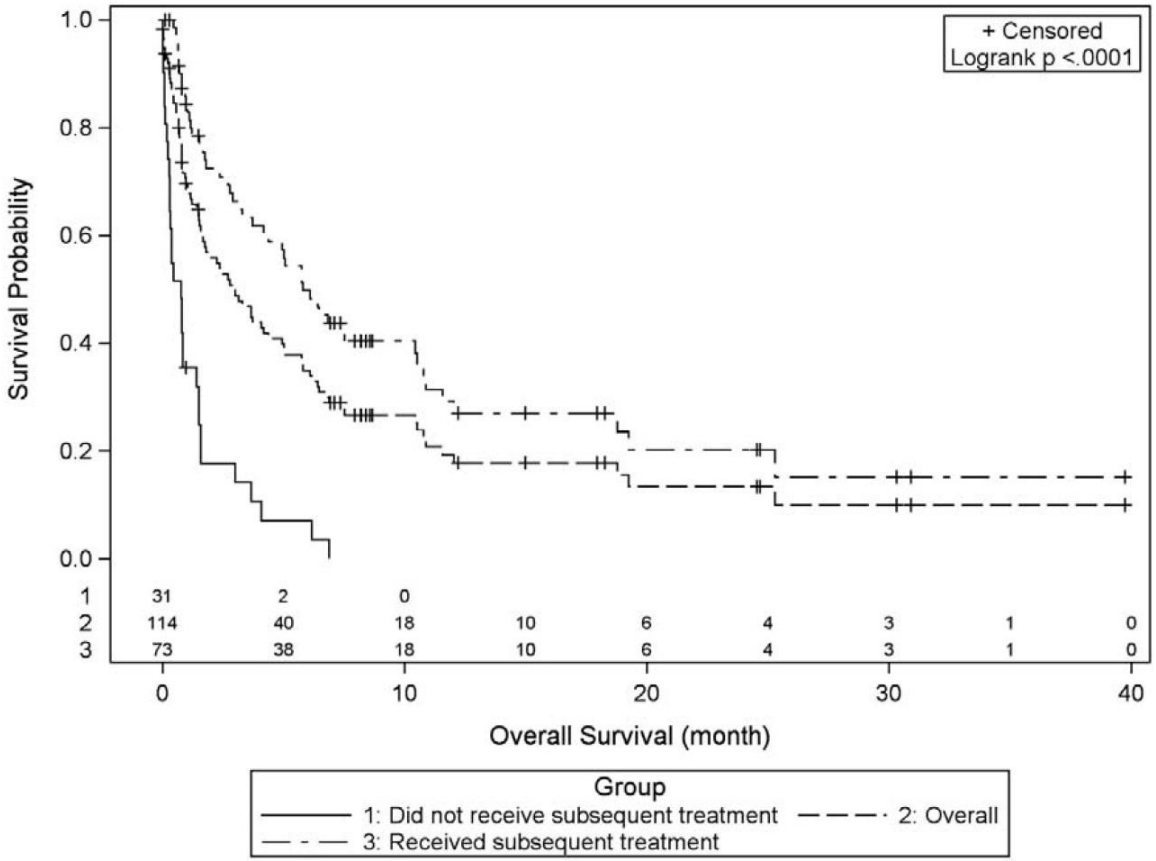
OS



Clinical risk factors and number of prior lines predict outcome in R/R MCL

MCL, mantle cell lymphoma; OS, overall survival; PFS, progression-free survival

Relapsed mantle cell lymphoma
Failure under ibrutinib



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Martin, Blood 2016

European MCL Network
Study generation 2018

< 65 years	> 60 years	> 65 years
MCL younger: R-CHOP/DHAP =>ASCT R-CHOP/DHAP+I =>ASCT => I R-CHOP/DHAP + I => I	*MCL elderly R2:* R-CHOP vs R-CHOP/Ara-C => Rituximab M +/- Lenalidomide	*MCL elderly I:* BR +/- Ibrutinib => Rituximab M +/- Ibrutinib

Relapse

Ibrutinib/Bortezomib	R-HAD +/- Bortezomib	Ibrutinib +/- ABT-199

Acknowledgements

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European MCL Network

GLA German Lymphoma Alliance