Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche	x						
Amgen	x						
InCyte	x						

VII CORSO del GRUPPO ITALIANO DI EMATOPATOLOGIA

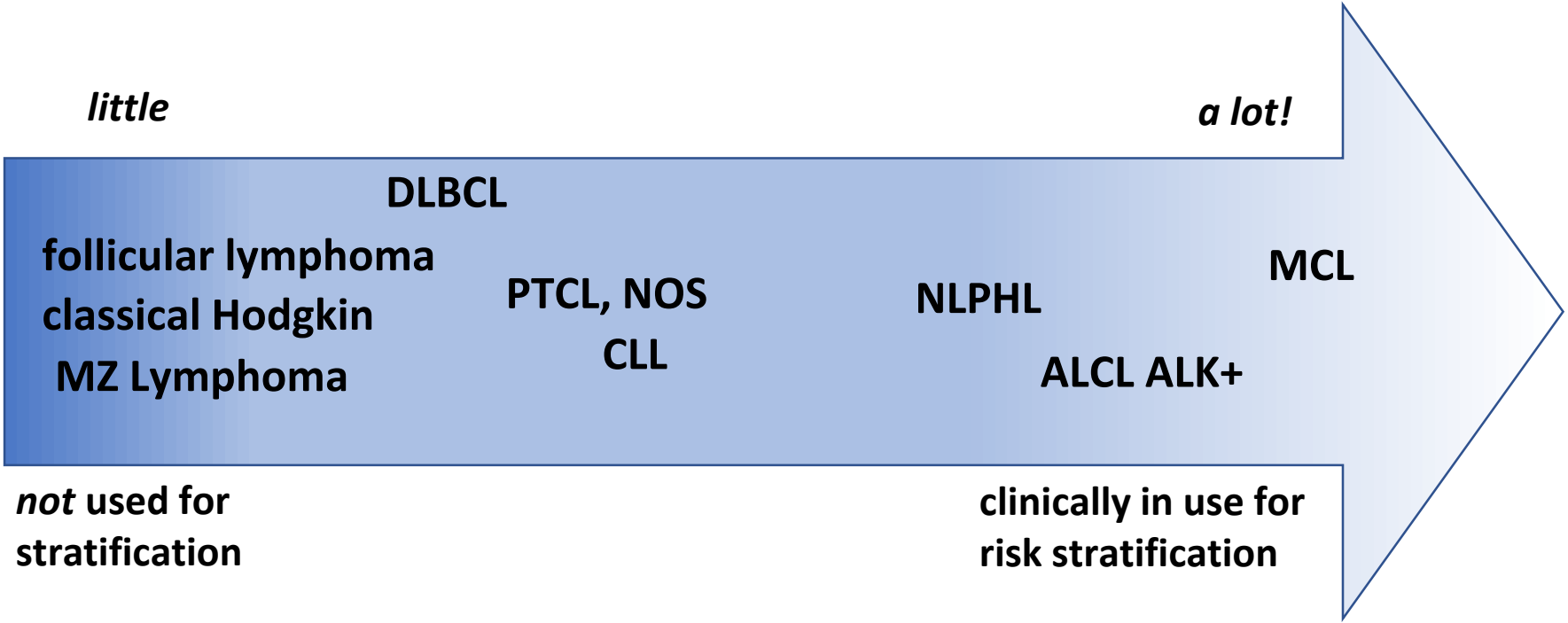
La DIAGNOSTICA EMATOPATOLOGICA nell'ERA della MEDICINA di PRECISIONE

MCL – can pathology tell prognosis?

Wolfram Klapper
Kiel, Germany

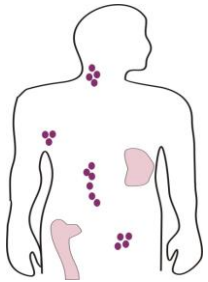
Bologna, Aula Prodi | 11-12 maggio 2026

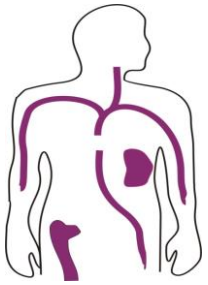
How much prognostic information does pathology provide?



MCL – can pathology tell prognosis?

Yes – by diagnosis

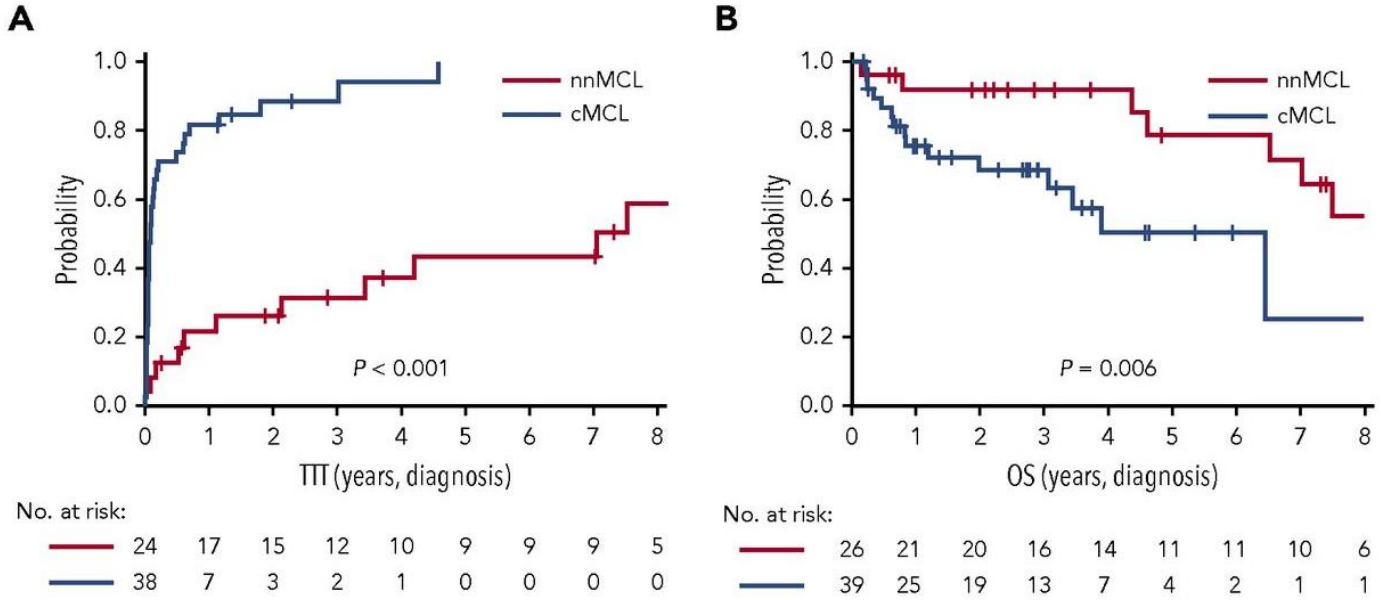




	conventional MCL	leukemic non-nodal MCL
Tissue involvement	primary nodal	Spleen, blood, bone marrow (CLL-like)
cytology	variable	usually non-blastic
CD5	93% +	64% +
Sox11	>90% positive	>90% negative
VH-hypermutation >5%	20%	70%
> 2 genomic imbalances	87%	0%

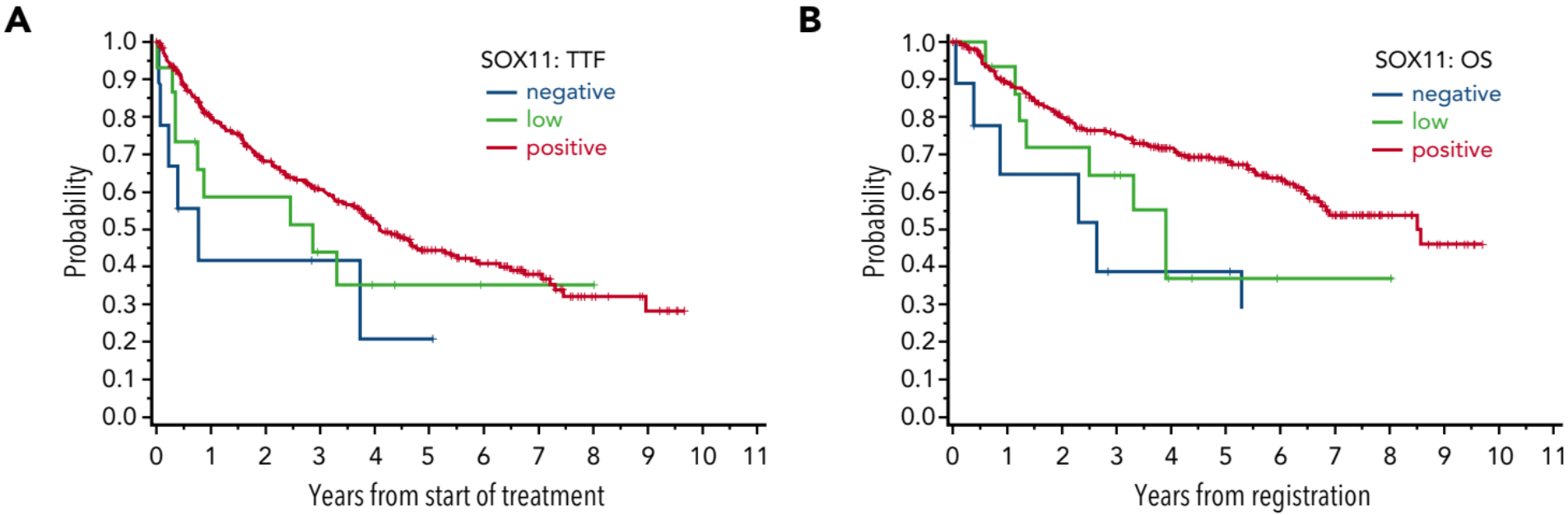
Modified according to Fernàndez et al , Cancer Res 2010

Leukemic non-nodal MCL –
a diagnostic subtype associated with prognosis



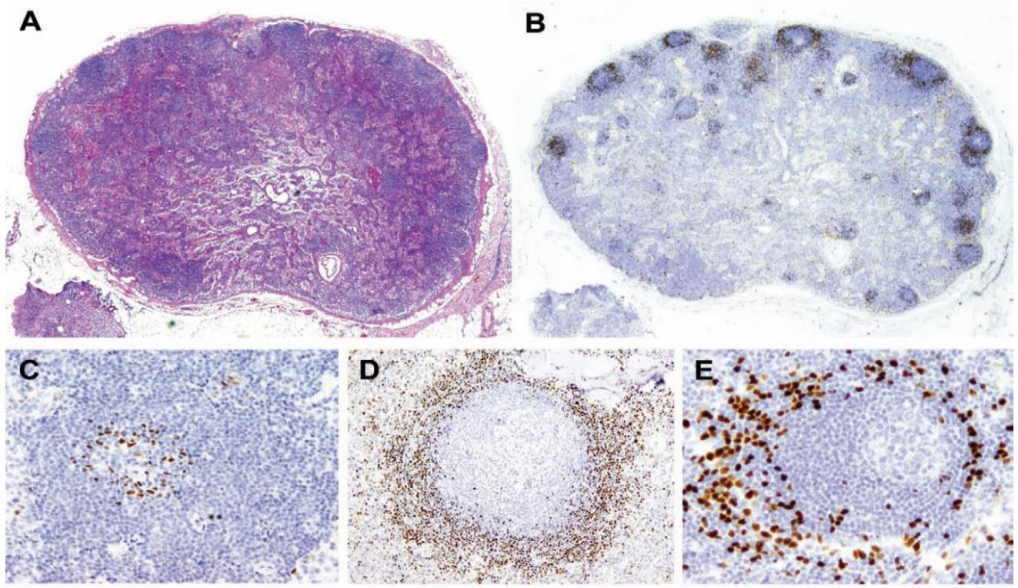
Clot et al. Blood 2028

SOX11 is not a stand-alone prognostic marker



Aukema et al. Blood 2018

In situ MCL neoplasia – a diagnostic subtype associated with prognosis



Carvajal-Cuenca, Haematologica 2012

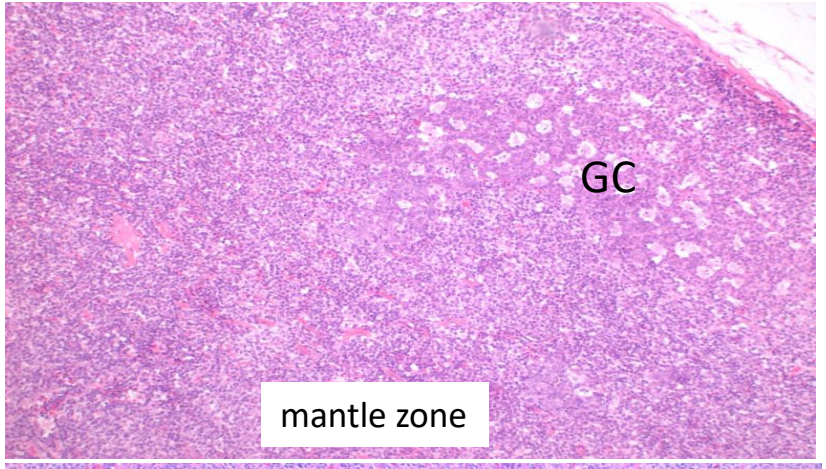
- Incidental finding
- staging requires exclusion of fully developed MCL at other site
- variable progression to ouvert disease reported

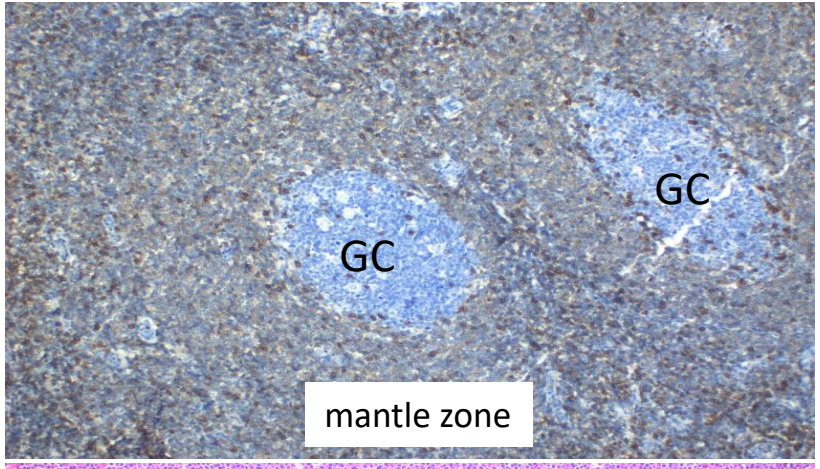
	Mantle zone growth of MCL	*In situ* Mantle cell Neoplasia
Lymph node architecture	Altered by expanded follicle mantle zones	Morphologically inconspicuous
Follicle mantle zone	• Most mantle zones affected. • Expanded mantle zones • Mantle zones mostly completely replaced by neoplastic cells.	• Few/focal affected mantles • Mantle zones **not expanded**. • **Partial replacement of mantle zones** by neoplastic cells (mostly inner part of mantle, rarely in the germinal center).
Accompanying growth pattern	Frequent additional nodular or diffuse growth of MCL	**No other growth pattern detectable**.
Clinical presentation	• Relatively frequent presentation of MCL. • Mostly multifocal lymphadenopathy with or without leukemic spread and/or bone marrow involvement.	• **Rare** • **Incidental finding** in lymph nodes analyzed due to an unrelated disease or benign hyperplasia. • Most cases **without involvement of blood and bone marrow**.

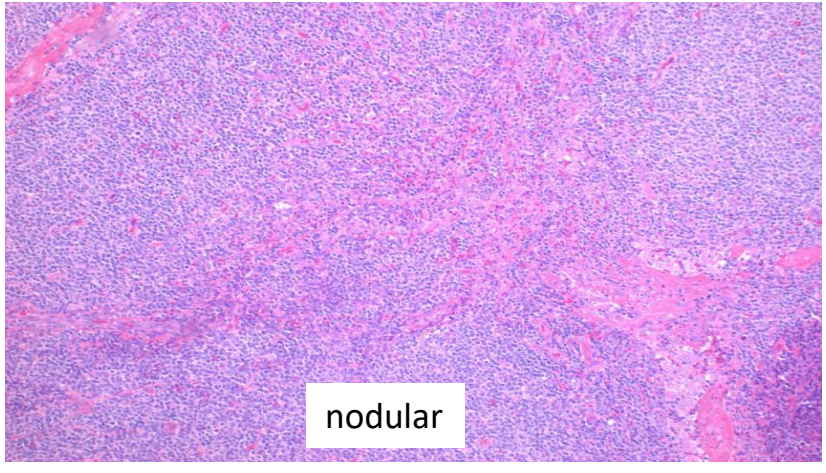
MCL – can pathology tell prognosis?

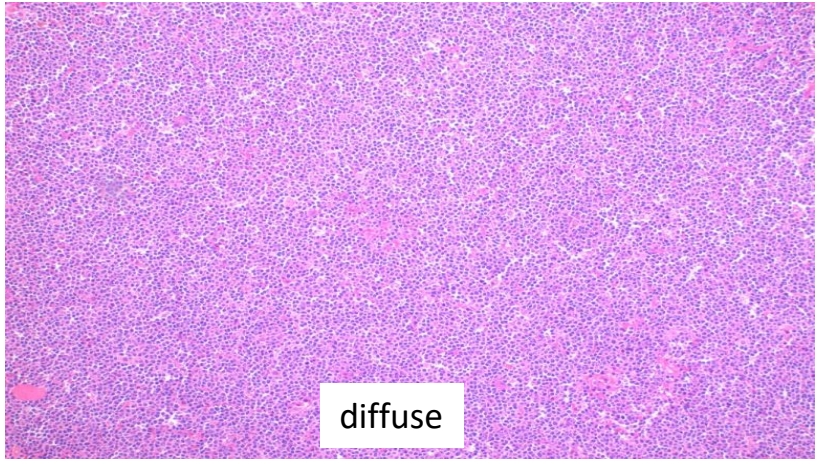
- Yes – by the diagnosis ✓ ➡
  - Mantel cell Lymphoma
  - leukemic non-nodal MCL
  - *In situ* Mantle cell Neoplasia
- Yes – …
- Yes – …
- Yes – …
- Yes – …

MCL growth pattern

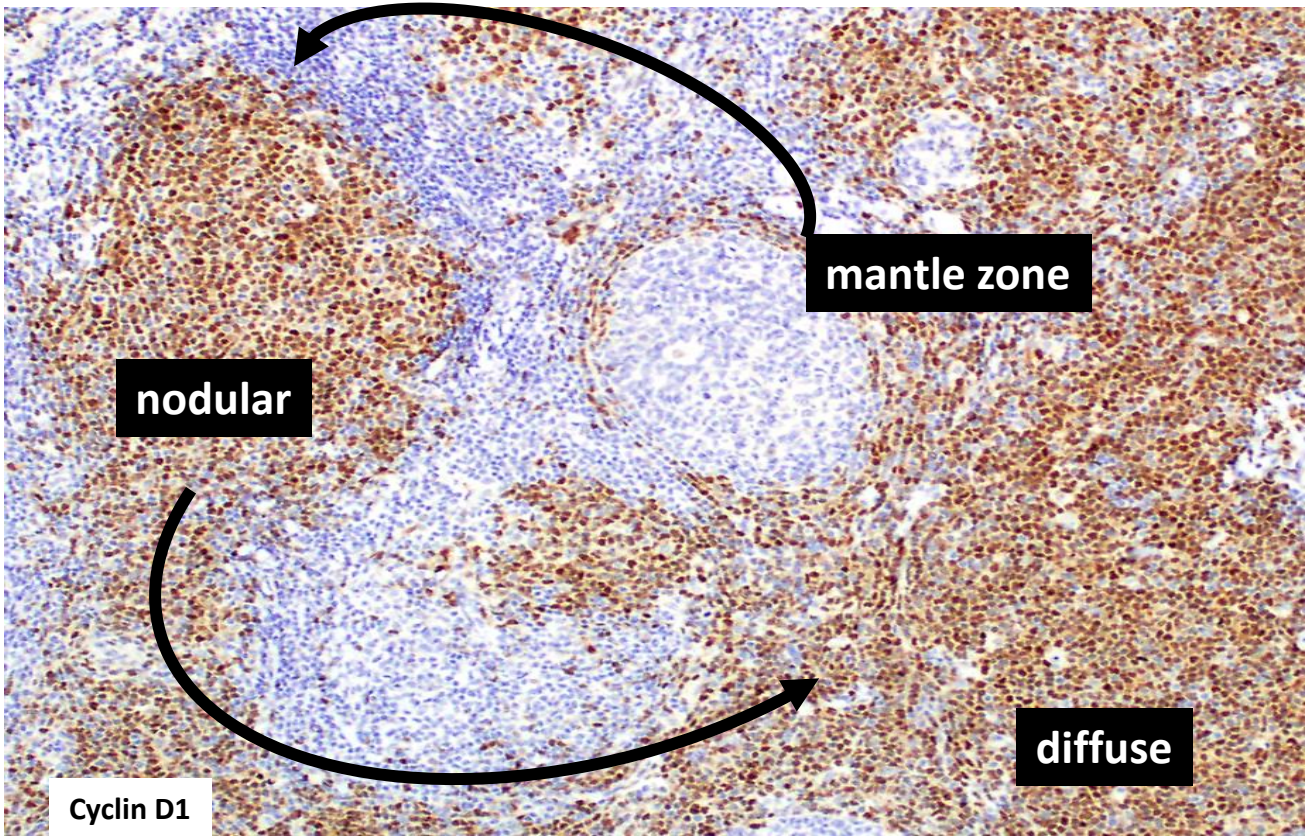








MCL evolution



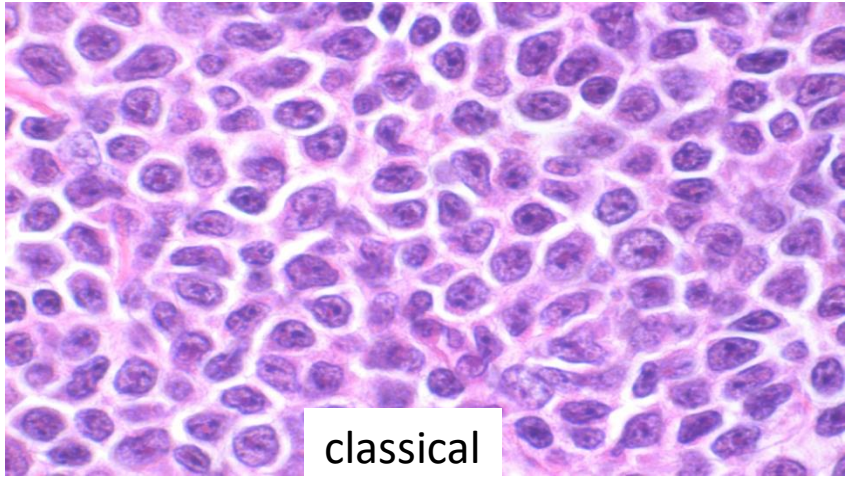
biopsy at diagnosis
mantle zone/nodular

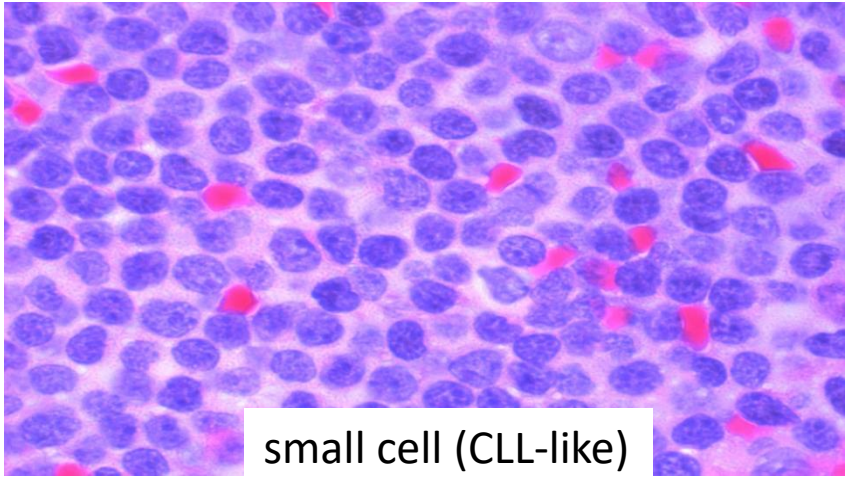
44%

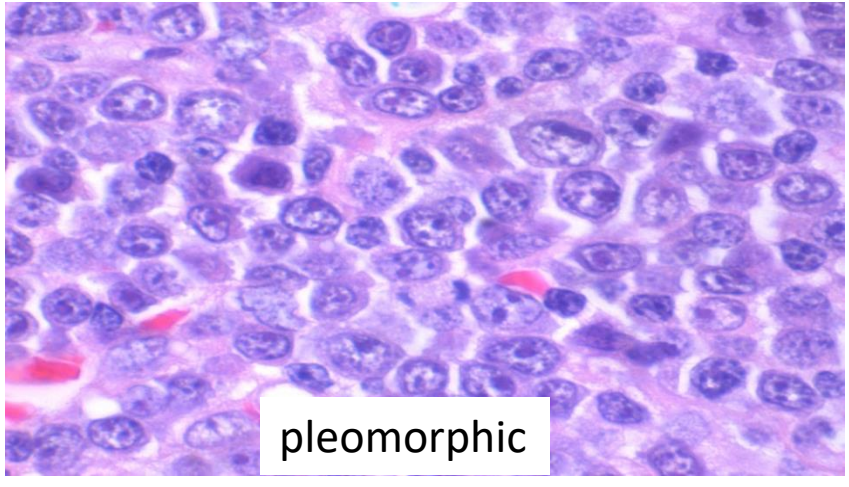
biopsy at relapse
diffuse

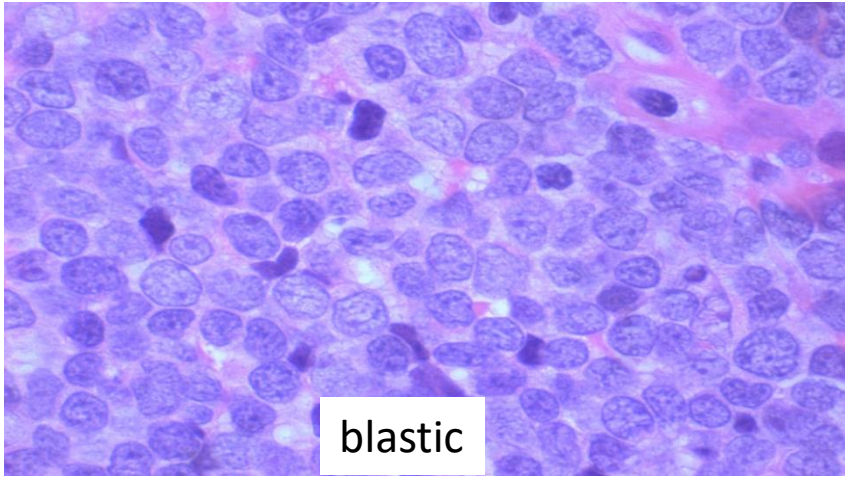
Histopathology 2013, **62**, 334–342.

Cytology of MCL

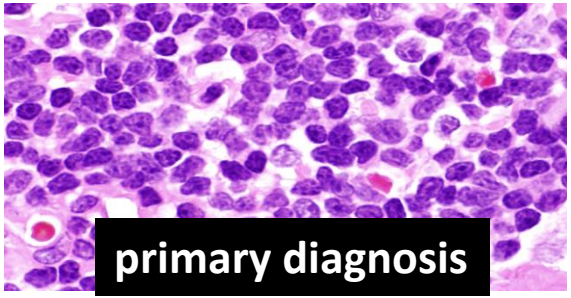


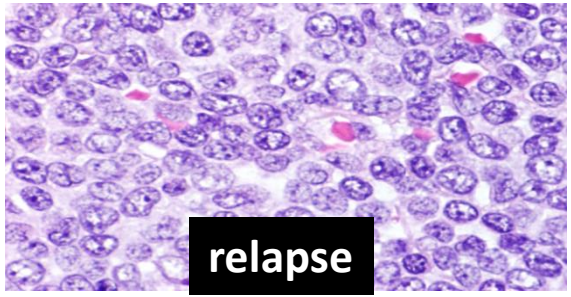


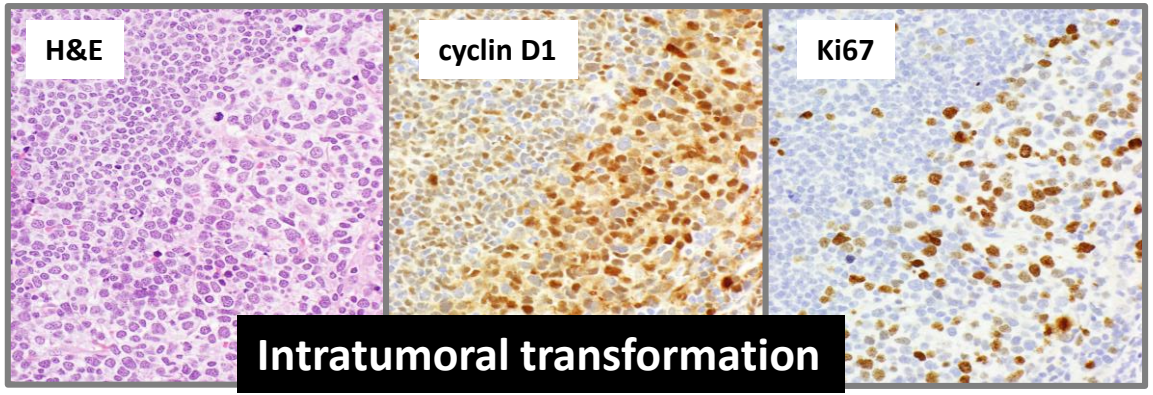




MCL evolution







biopsy at diagnosis
small cell/classical

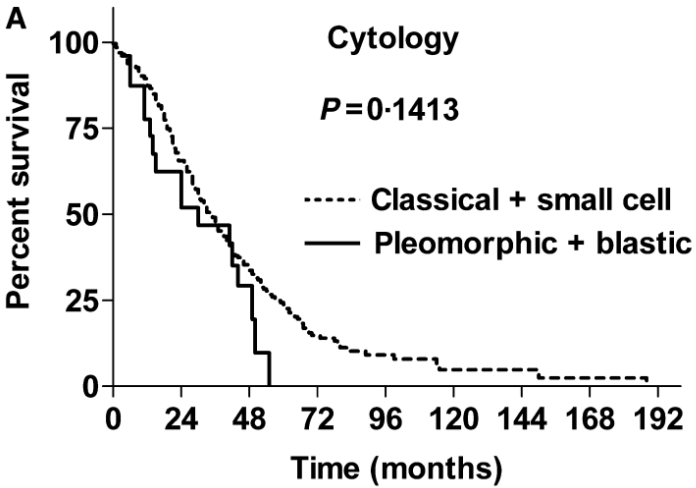
22%

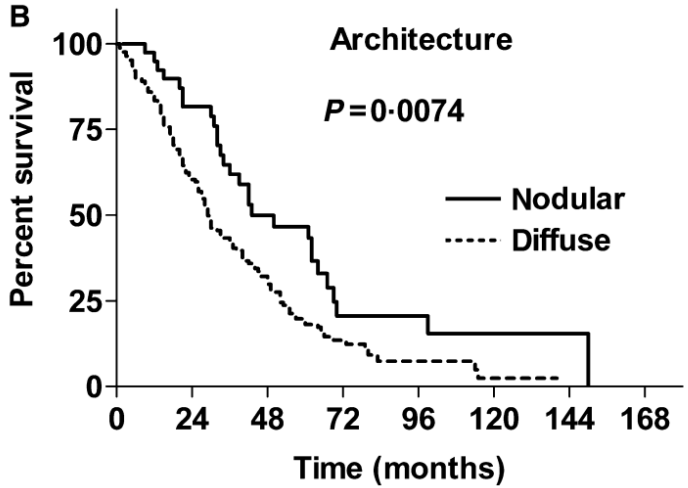
biopsy at relapse
blastoid

Histopathology 2013, **62**, 334–342.

MCL – can pathology tell prognosis?

Yes – by morphology





Tiemann, Br J Haematol 2005

MCL – can pathology tell prognosis?

- Yes – by the diagnosis
- Yes – by morphology ✓ → classical/small cell versus blastic/pleomorphic cytology
- Yes – …
- Yes – …
- Yes – …

The clinical risk score MIPI

By using this calculator you accept that the European MCL Network does not assume any liability.

MIPI/MIPI-c	MIPI	
Age		years
ECOG PS	please select	
LDH		U/L or µkat/L
LDH-ULN		U/L or µkat/L
WBC count		G/L
MIPI score	---	

Please select a value for Age...

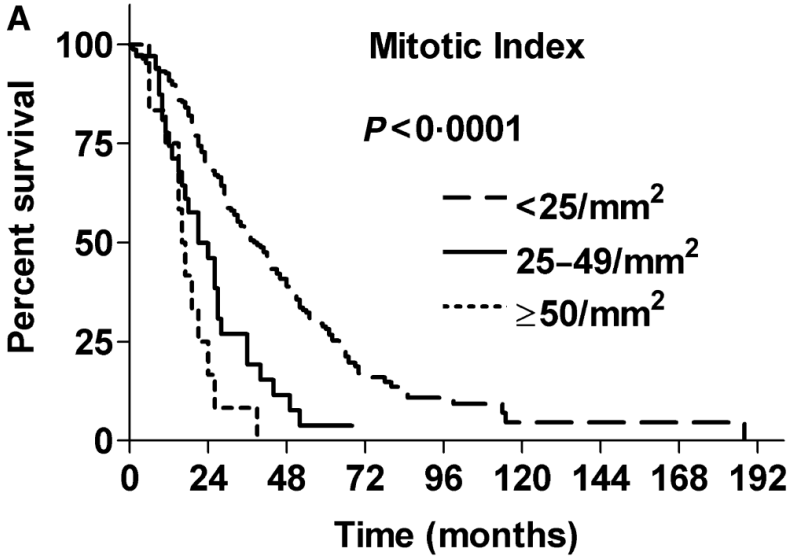
(c) 2016 European MCL Network

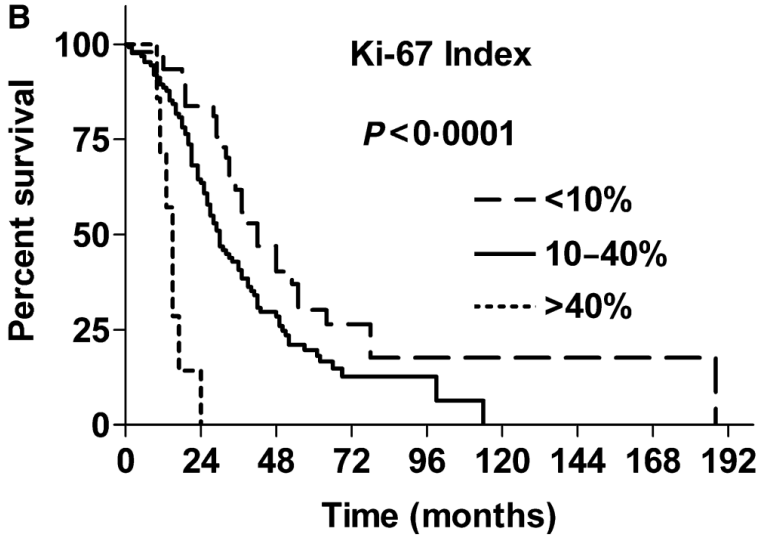
https://www.european-mcl.net/home/scores-mipi-mipi-c-19.html

EUROPEAN mcl NETWORK

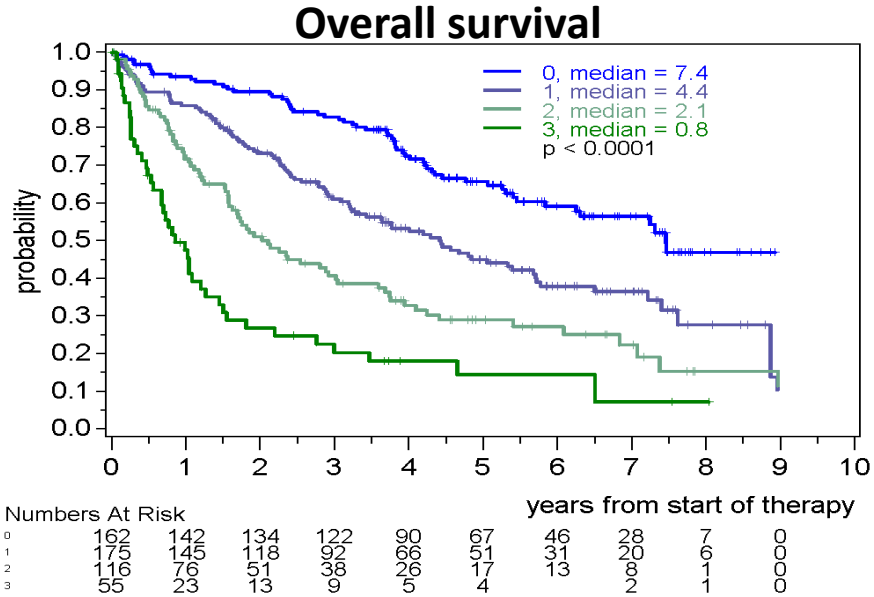
MCL – can pathology tell prognosis?

Yes – by proliferation





MIPI and Ki67 in „MCL Younger“ and „MCL Elderly“



MIPI low, Ki67 <30%

MIPI low, Ki67>30%
MIPI intermediate, Ki67<30%

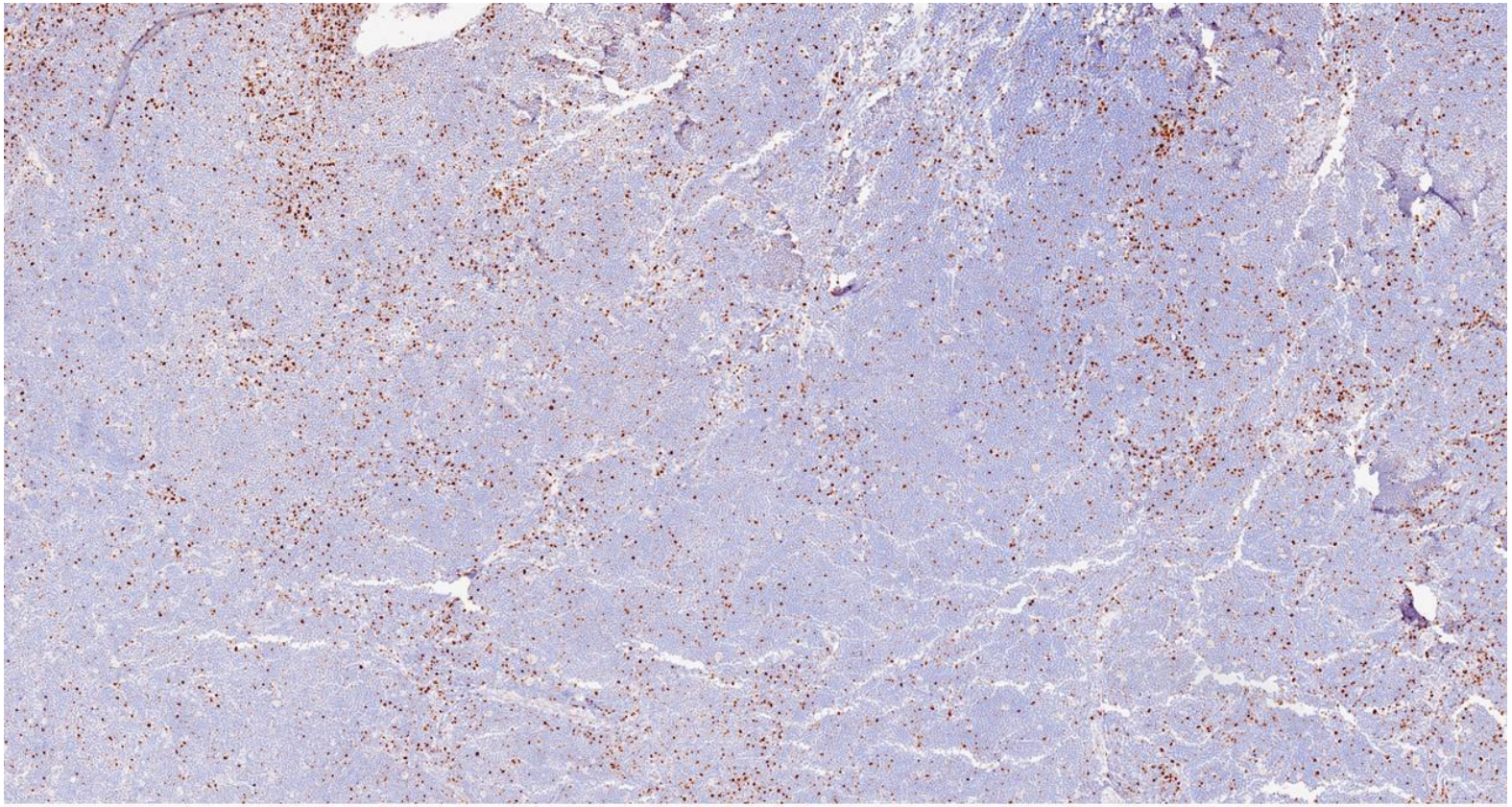
MIPI high, Ki67<30%
MIPI intermediate, Ki67>30%

MIPI high, Ki67 >30%

Hoster et al, JCO 2016

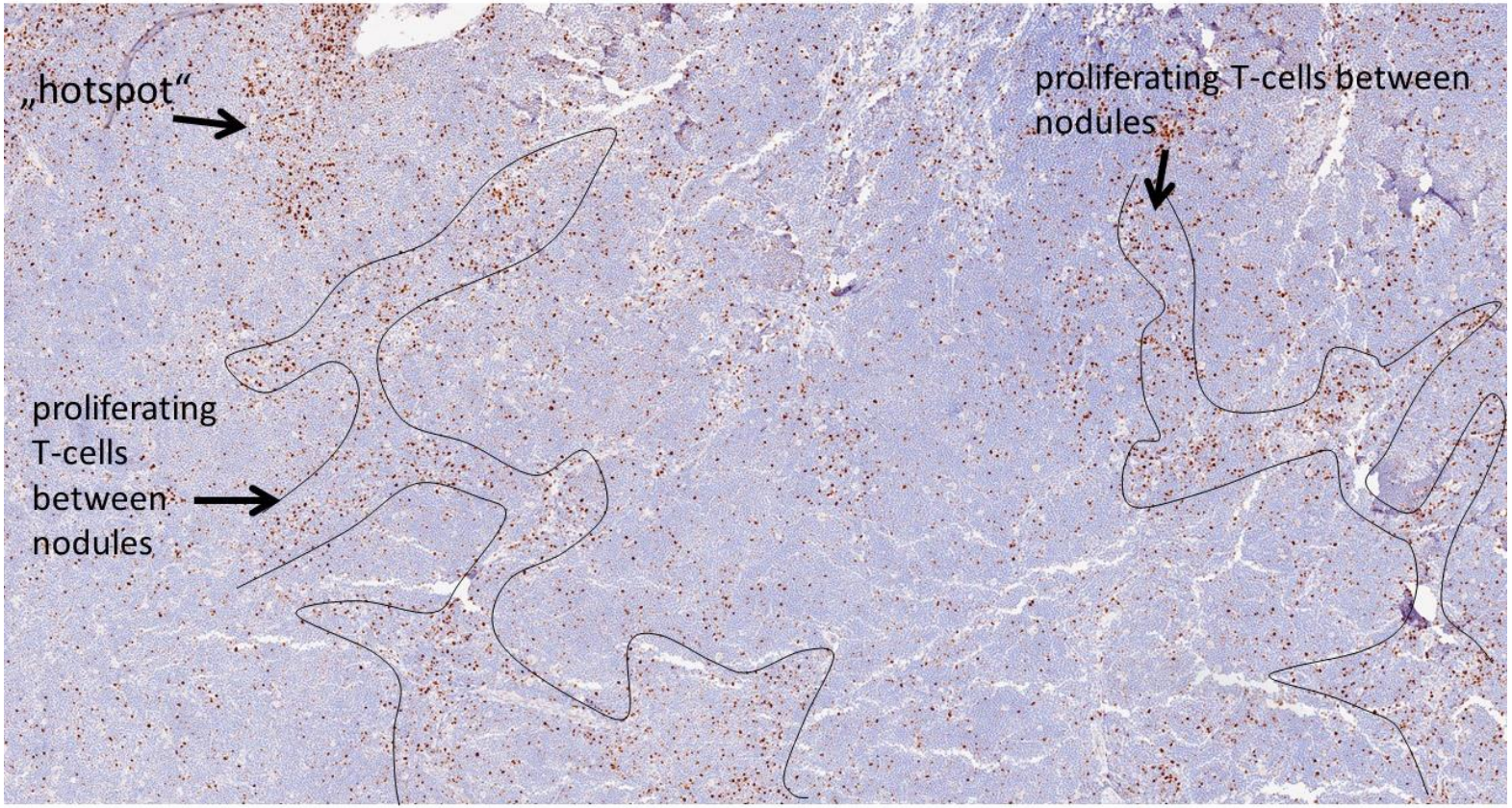
Assessing Ki67 in MCL

Identify areas free of “hot-spots” or proliferating T-cells



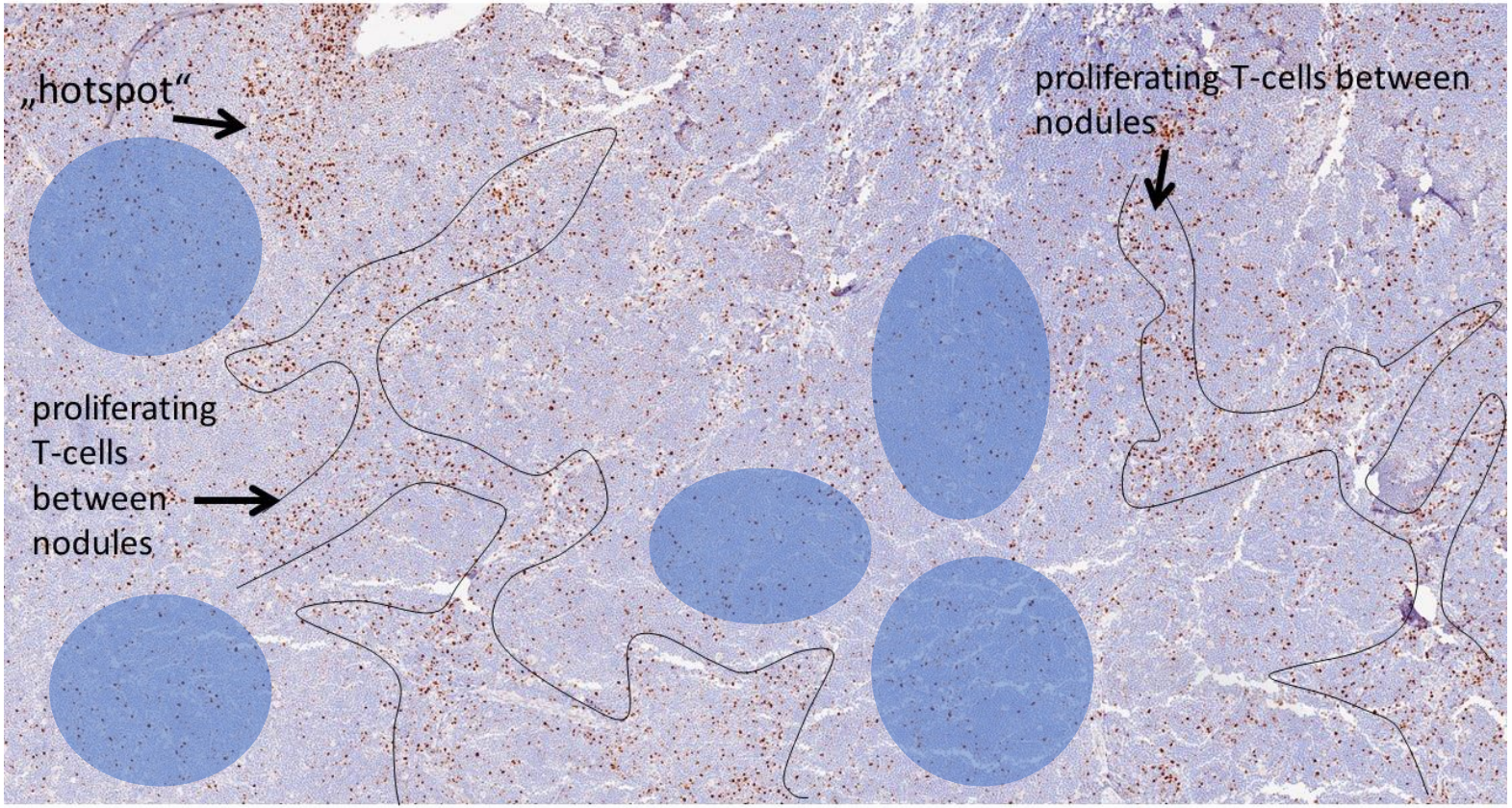
Assessing Ki67 in MCL

Identify areas free of “hot-spots” or proliferating T-cells



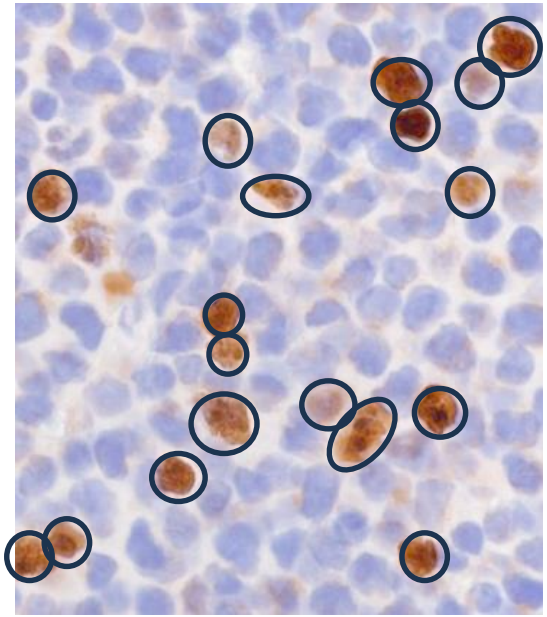
Assessing Ki67 in MCL

Identify areas free of “hot-spots” or proliferating T-cells

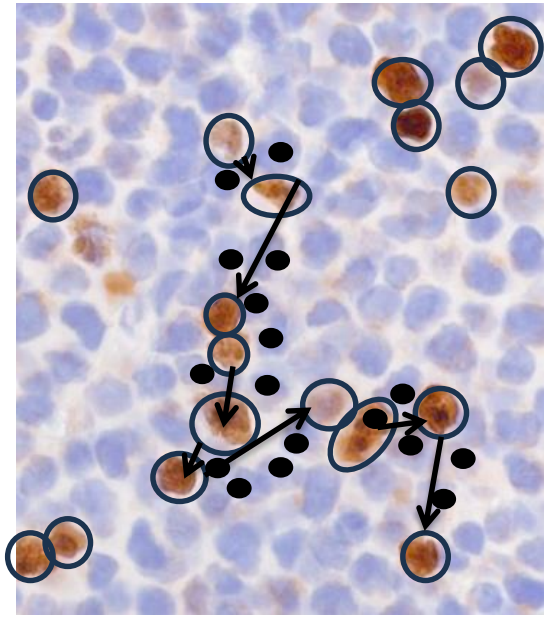


Assessing Ki67 in MCL

count 2 x 100 cells
(each 100 in an independent area)

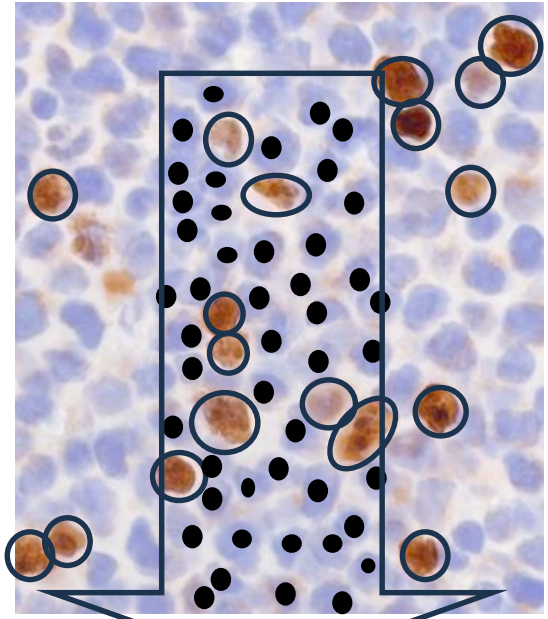


37%



wrong!

15%



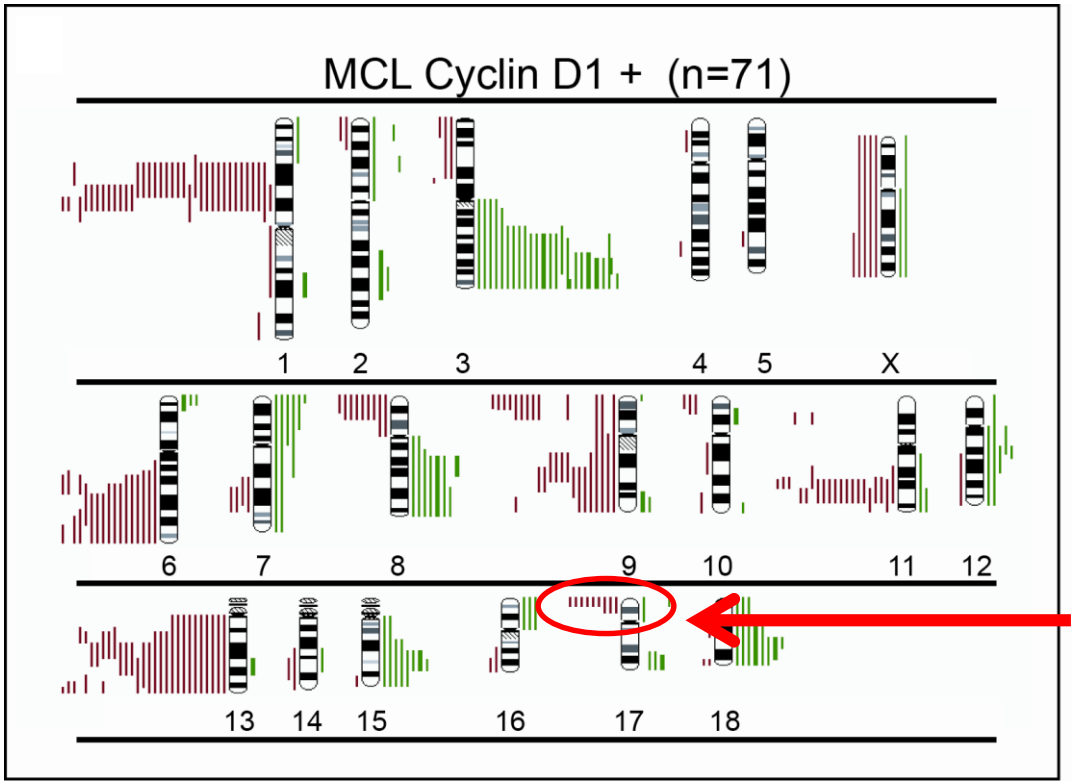
correct!

MCL – can pathology tell prognosis?

- Yes – by the diagnosis
- Yes – by morphology
- Yes – by Proliferation ✓
- Yes – ...
- Yes – ...

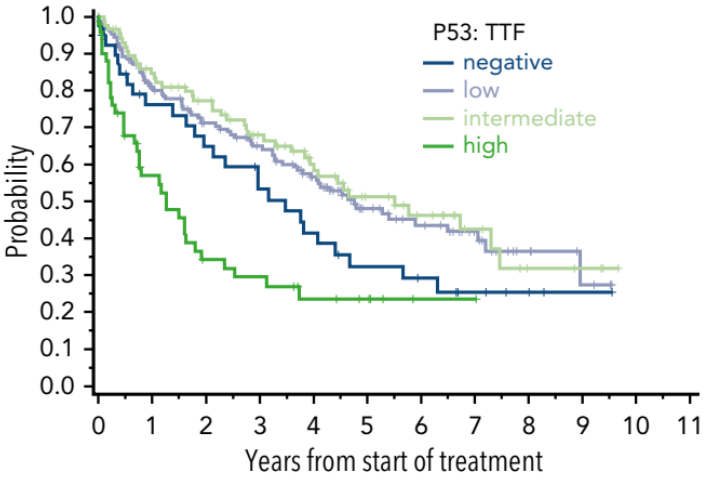
Ki67 reported according to guidelines

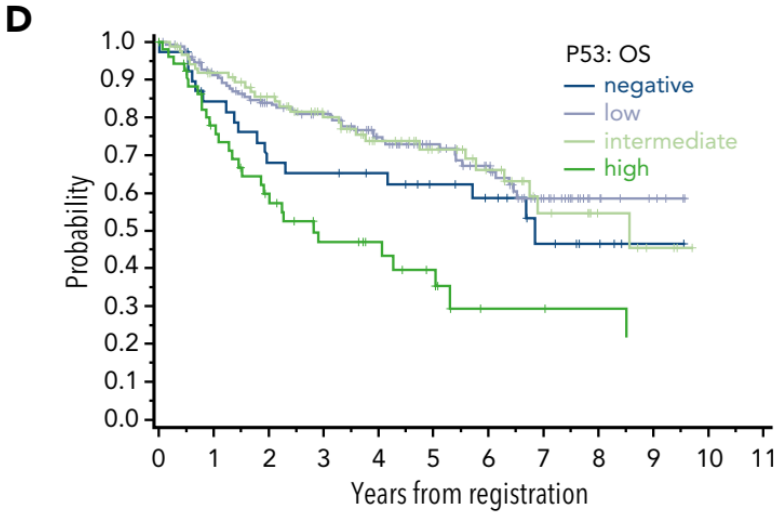
MCL - frequent secondary genetic changes



Salaverria et al. J Clin Oncol 2007

p53 expression and survival

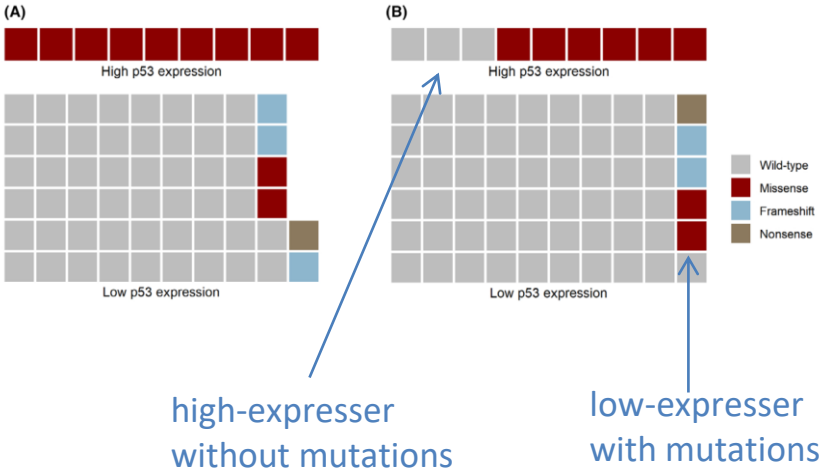




Aukema et al. Blood 2018

What is better p53 immunohistochemistry of genetic testing?

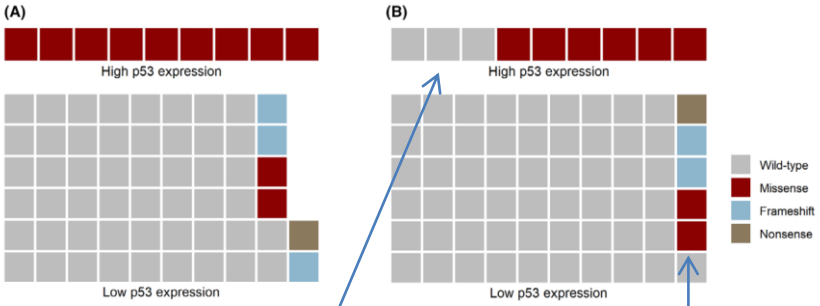
Both methods correlate but not by 100%



Rodrigues, Br. J Haematol 2020

What is better p53 immunohistochemistry of genetic testing?

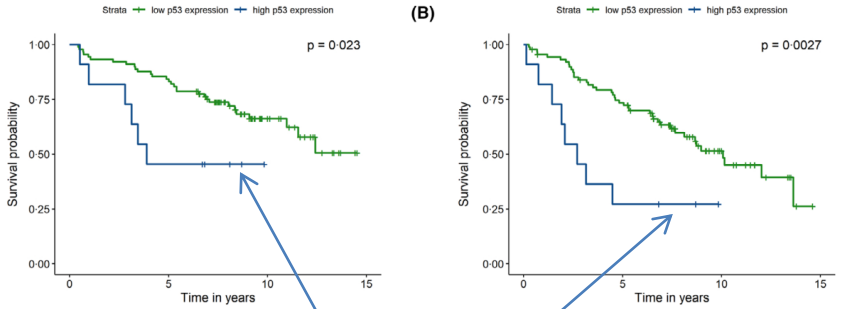
Both methods correlate but not by 100%



high-expresser without mutations

low-expresser with mutations

Both methods erroneously may assign high-risk



long-term survival despite mutations

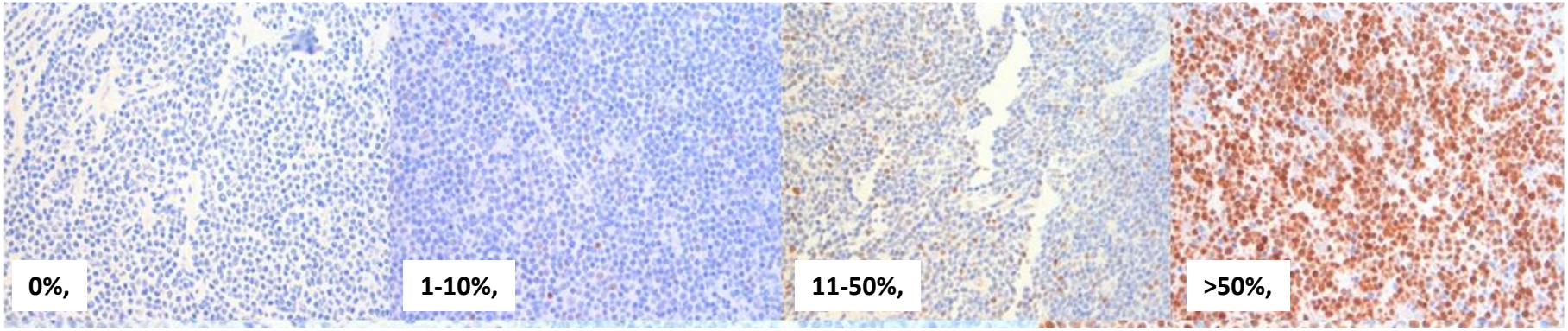
Rodrigues, Br. J Haematol 2020

Virchows Archiv
https://doi.org/10.1007/s00428-020-02750-7

ORIGINAL ARTICLE

Reproducibility of histologic prognostic parameters for mantle cell lymphoma: cytology, Ki67, p53 and SOX11

Giorgio A. Croci[1,2,3] · Eva Hoster[4,5] · Sílvia Beà[6,7] · Guillem Clot[6,7] · Anna Enjuanes[6,7] · David W. Scott[8] · José Cabeçadas[9] · Luis Veloza[10] · Elias Campo[6,7,10] · Erik Clasen-Linde[11] · Rashmi S. Goswami[12] · Lars Helgeland[13] · Stefano Pileri[14] · Grzegorz Rymkiewicz[15] · Sarah Reinke[1] · Martin Dreyling[5] · Wolfram Klapper[1]



>50% TP53 staining means .... ***strong and homogeneous staining***.
Weak and heterogeneous staining is frequently found in lymphomas without mutation.

MCL – can pathology tell prognosis?

- Yes – by the diagnosis
- Yes – by morphology
- Yes – by Proliferation
- Yes – by TP53 ✓
- Yes – …

p53 expression (or mutation/deletion) reported according to guideline

MCL – can pathology tell prognosis?

- Yes – by the diagnosis
- Yes – by morphology
- Yes – by Proliferation
- Yes – by TP53
- Yes – by AI

your diagnostic report is packed with prognostic information:

DIAGNOSIS:
Mantle cell lymphoma, classical type
(Ki67 27%, p53 wild type pattern)

MCL – can pathology tell prognosis?

An your prognostic information is used for clinical decission making!

CAR-T-cell Treatment for Untreated High Risk MANtle Cell Lymphoma (CARMAN)

ClinicalTrials.gov ID NCT06482684

Sponsor Christian Schmidt, MD

Information provided by Christian Schmidt, MD, Ludwig-Maximilians - University of Munich (Responsible Party)

Last Update Posted 2024-07-01

your diagnostic report is packed with prognostic information:

DIAGNOSIS:

Mantle cell lymphoma, classical type

(Ki67 27%, p53 wild type pattern)

ACKNOWLEDGEMENTS

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Rainer Spang

Michael Huttner

Likas Wolfseher

Faculty of Informatics and Data Science (FIDS), University of Regensburg

EUROPEAN mCL NETWORK

LEUKEMIA & LYMPHOMA SOCIETY®

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- **Martin Dreyling**
- **All contributing pathologists**

GLA German Lymphoma Alliance

Andreas Rosenwald
German Ott
Hilka Rauert-Wunderlich