20 ANNI DI EMATOLOGIA A TREVISO

TREVISO | 18-20 NOVEMBRE 2021
Auditorium Fondazione Cassamarca

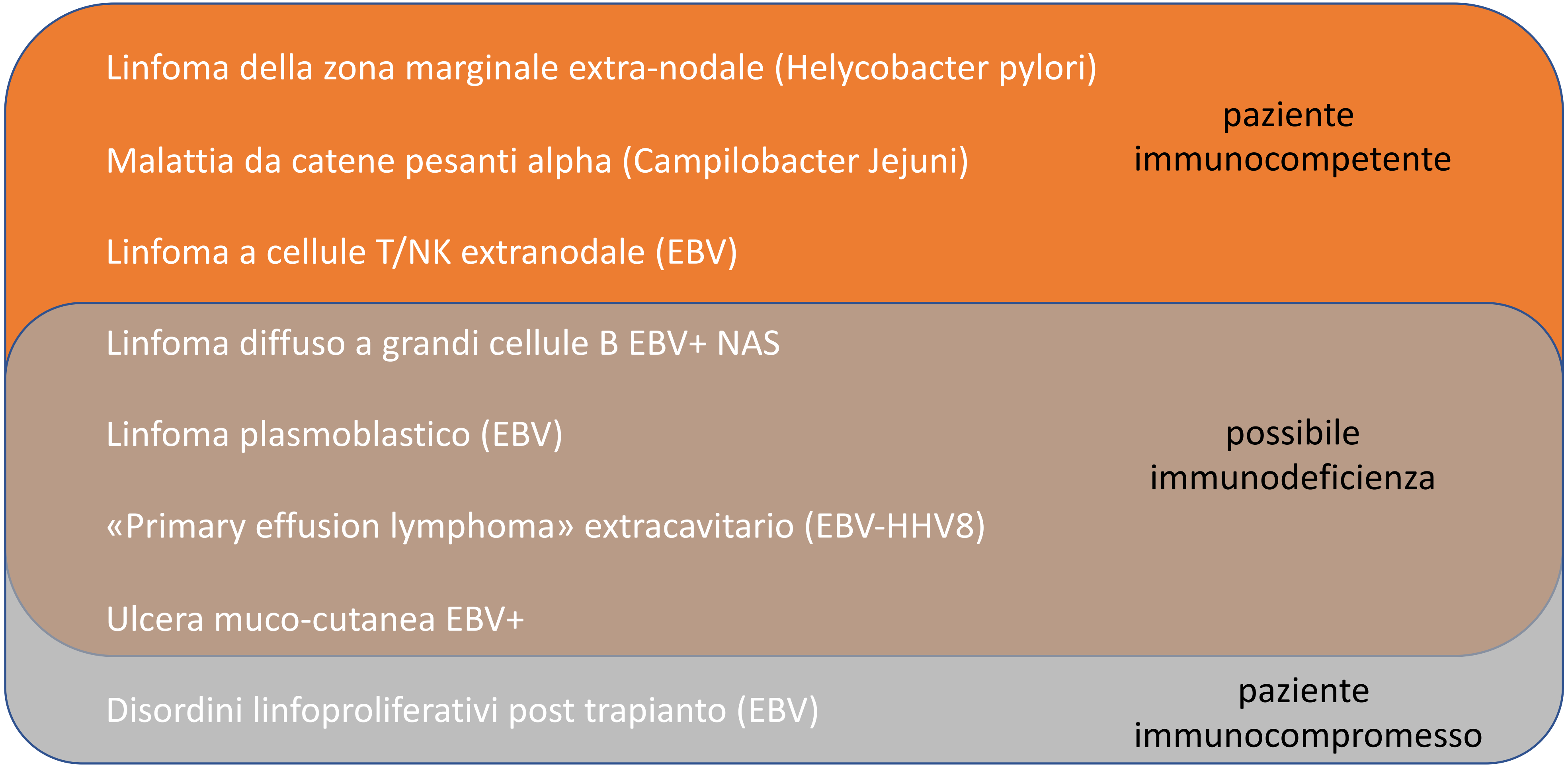
Le lesioni istopatologiche: dall’infezione al linfoma

Dr. Claudio Agostinelli
UO Emolinfopatologia IRCCS Azienda Ospedaliero-Universitaria di Bologna
Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna

Disclosures of Claudio Agostinelli:
nessun conflitto di interessi da dichiarare

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

Disordini linfoproliferativi correlati ad infezioni nel tratto gastroenterico



Linfoma della zona marginale extra-nodale (Helycobacter pylori)

Malattia da catene pesanti alpha (Campilobacter Jejuni)

Linfoma a cellule T/NK extranodale (EBV)

paziente
immunocompetente

Linfoma diffuso a grandi cellule B EBV+ NAS

Linfoma plasmoblastico (EBV)

«Primary effusion lymphoma» extracavitario (EBV-HHV8)

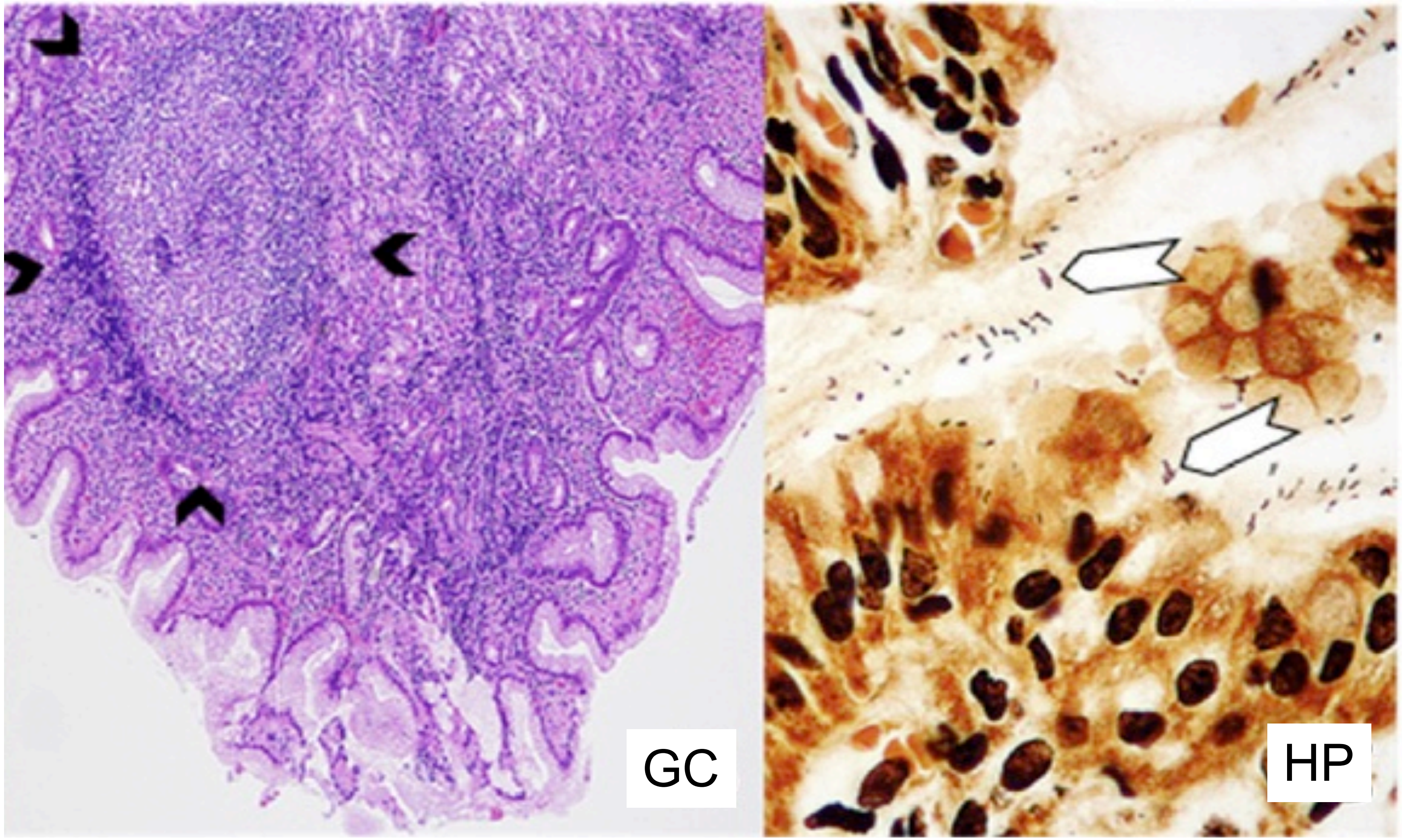
Ulcera muco-cutanea EBV+

possibile
immunodeficienza

Disordini linfoproliferativi post trapianto (EBV)

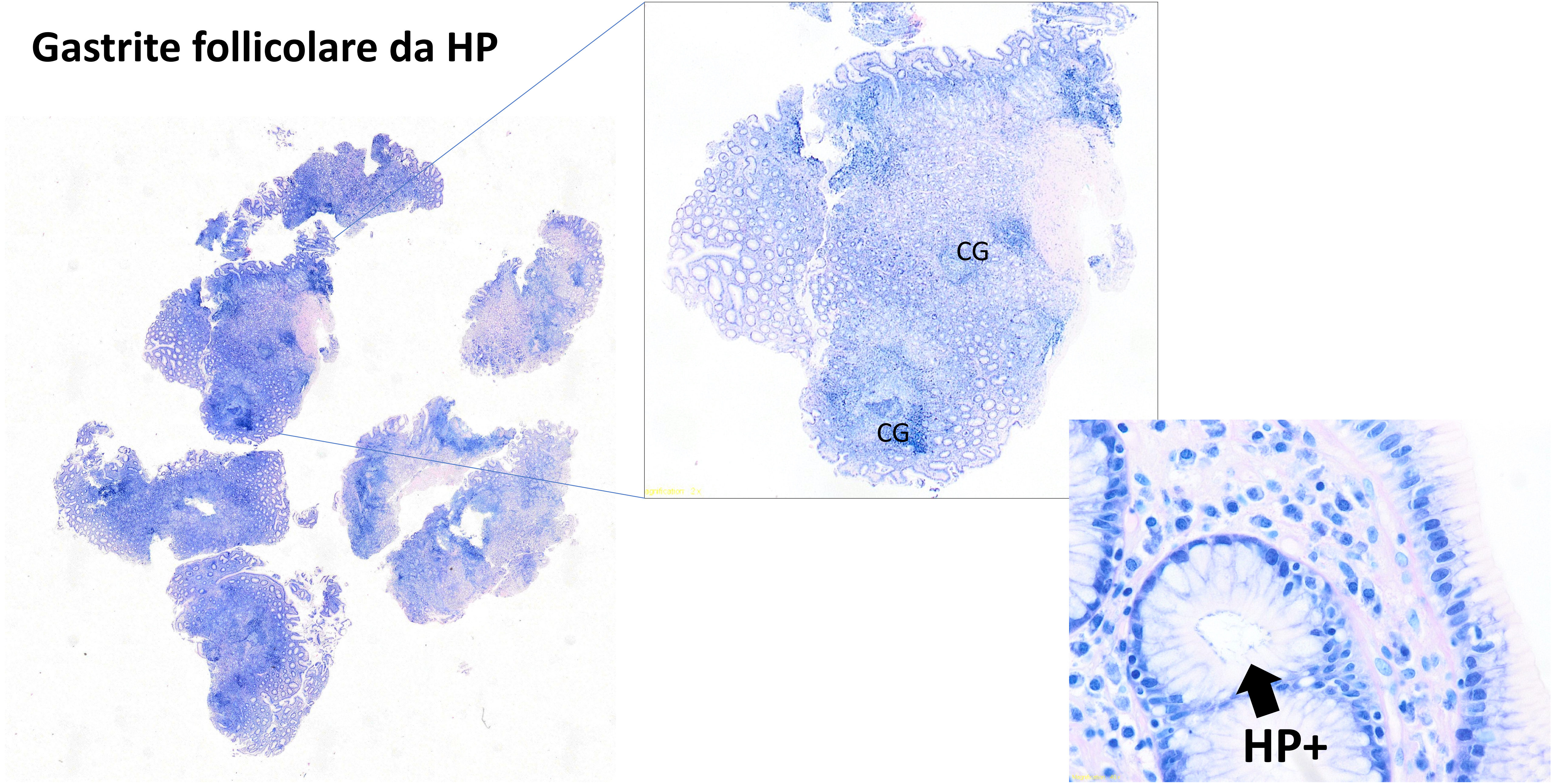
paziente
immunocompromesso

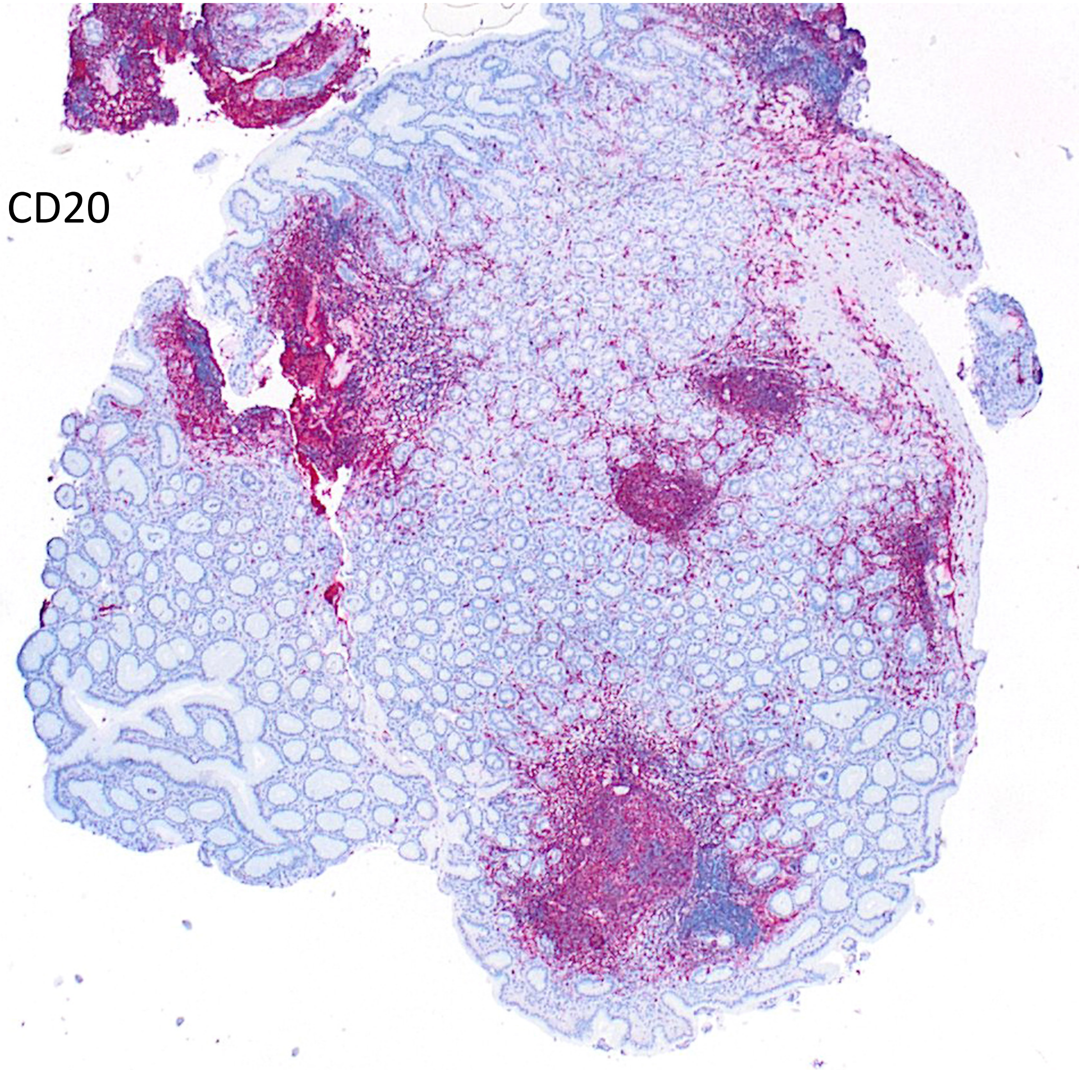
MALT in gastrite cronica *HP*

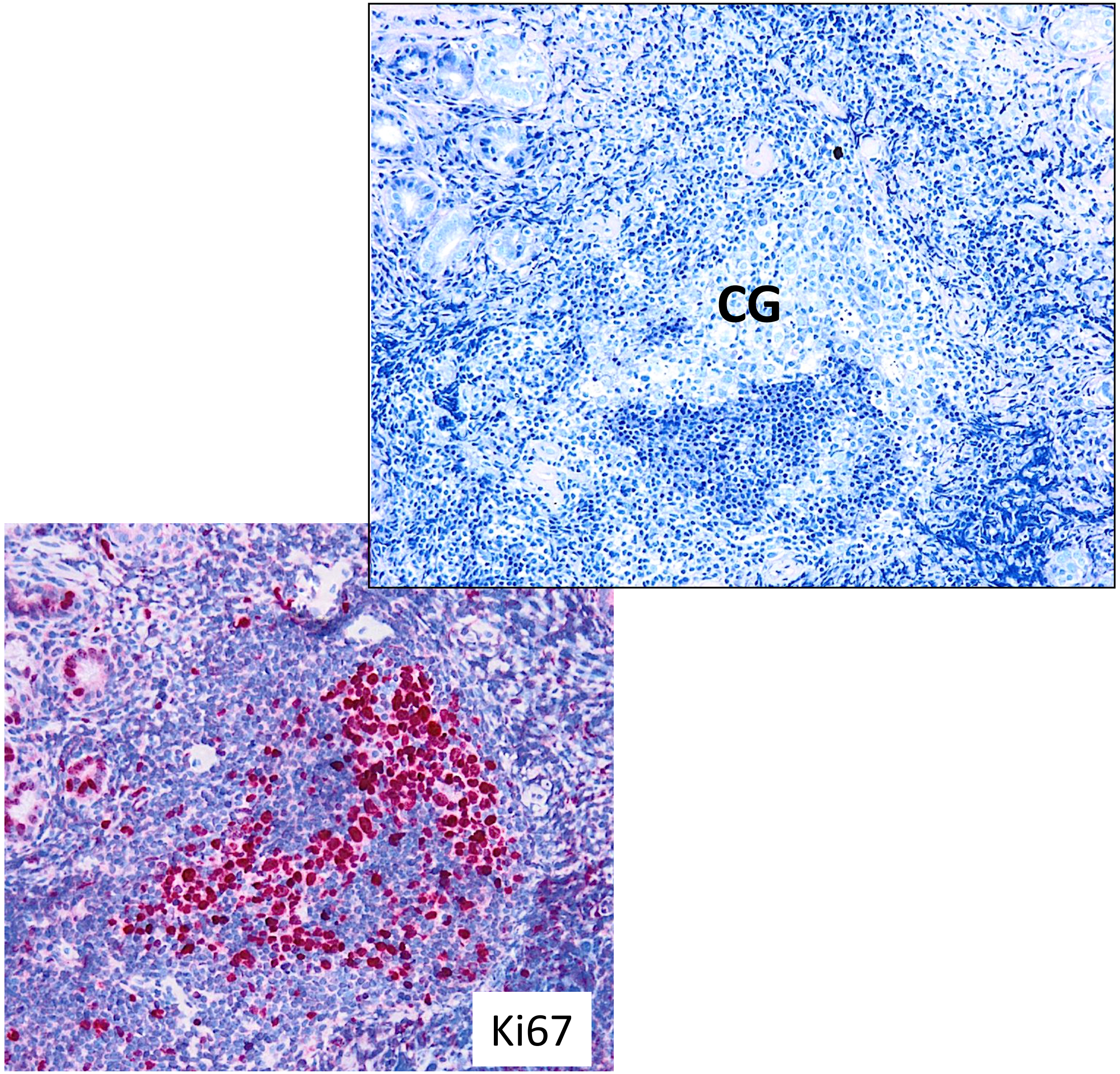


Varbanova Best & Practice Research Clinical Gastroenterology 2014

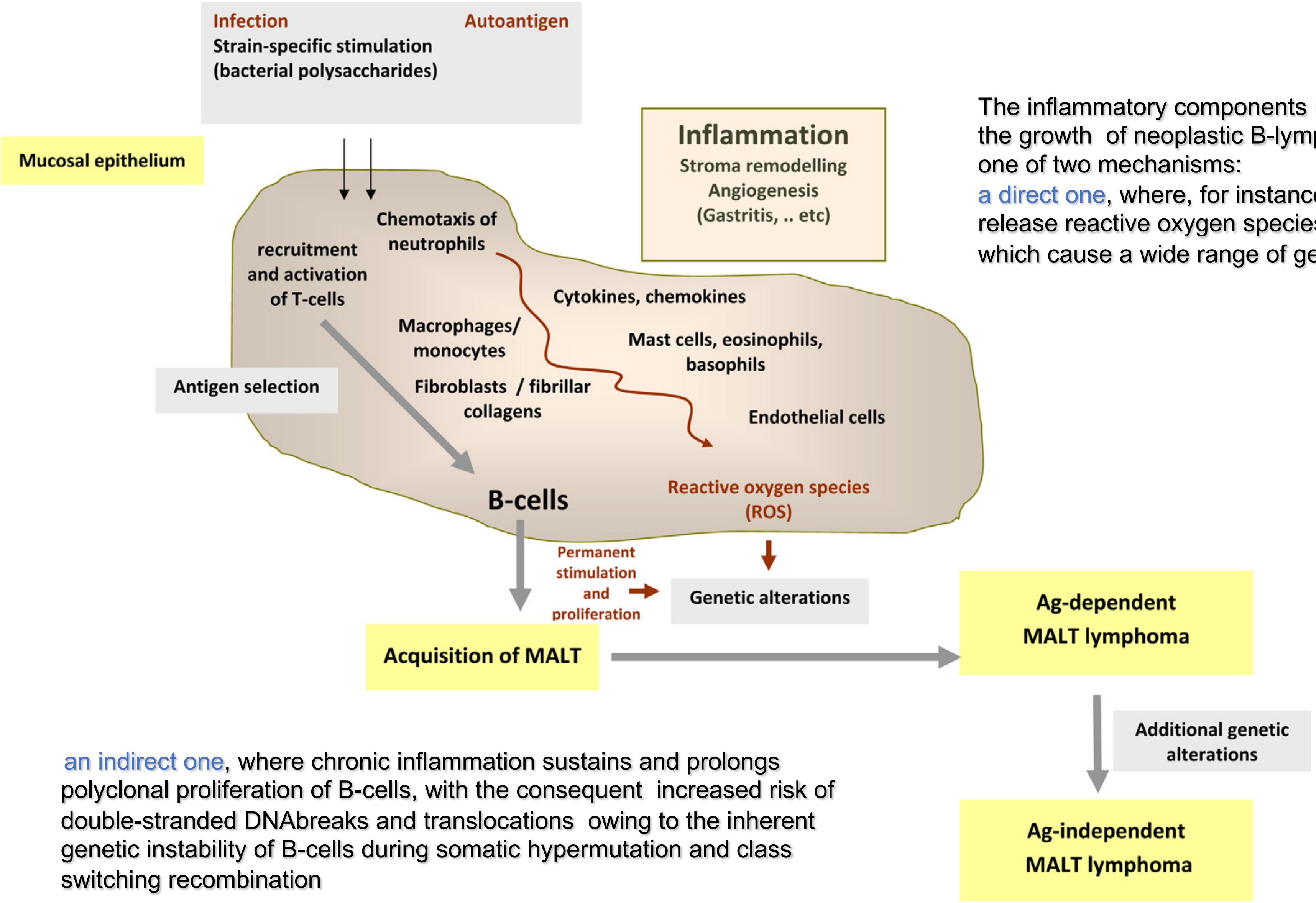
Gastrite follicolare da HP




CD20


CG
Ki67

chronic inflammation (chronic infection or autoimmune processes) sustained antigenic or auto antigenic stimulation not only triggers polyclonal B-cell proliferation, favours the assembly of aggregates of polyclonal B-lymphocytes but also recruits a series of inflammatory cells, including T-lymphocytes, macrophages and neutrophils, to the site of inflammation.



Infection

Autoantigen

Strain-specific stimulation (bacterial polysaccharides)

Mucosal epithelium

Inflammation

Stroma remodelling

Angiogenesis

(Gastritis, .. etc)

Chemotaxis of neutrophils

recruitment and activation of T-cells

Cytokines, chemokines

Macrophages/ monocytes

Mast cells, eosinophils, basophils

Antigen selection

Fibroblasts / fibrillar collagens

Endothelial cells

B-cells

Reactive oxygen species (ROS)

Permanent stimulation and proliferation

Genetic alterations

Acquisition of MALT

Ag-dependent MALT lymphoma

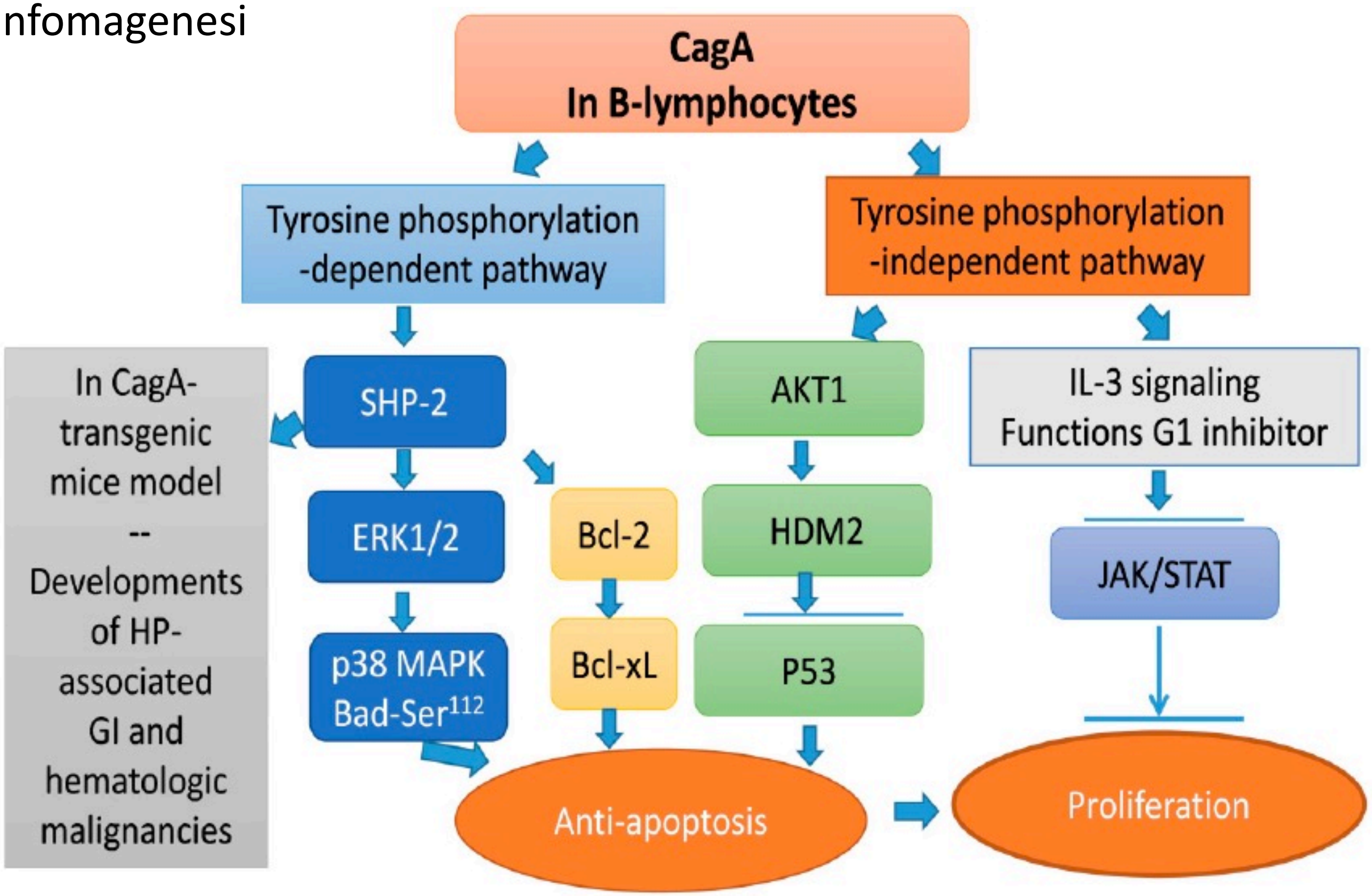
Additional genetic alterations

Ag-independent MALT lymphoma

The inflammatory components may promote the growth of neoplastic B-lymphocytes by either one of two mechanisms:
a direct one, where, for instance, neutrophils release reactive oxygen species (ROS),
which cause a wide range of genetic aberrations

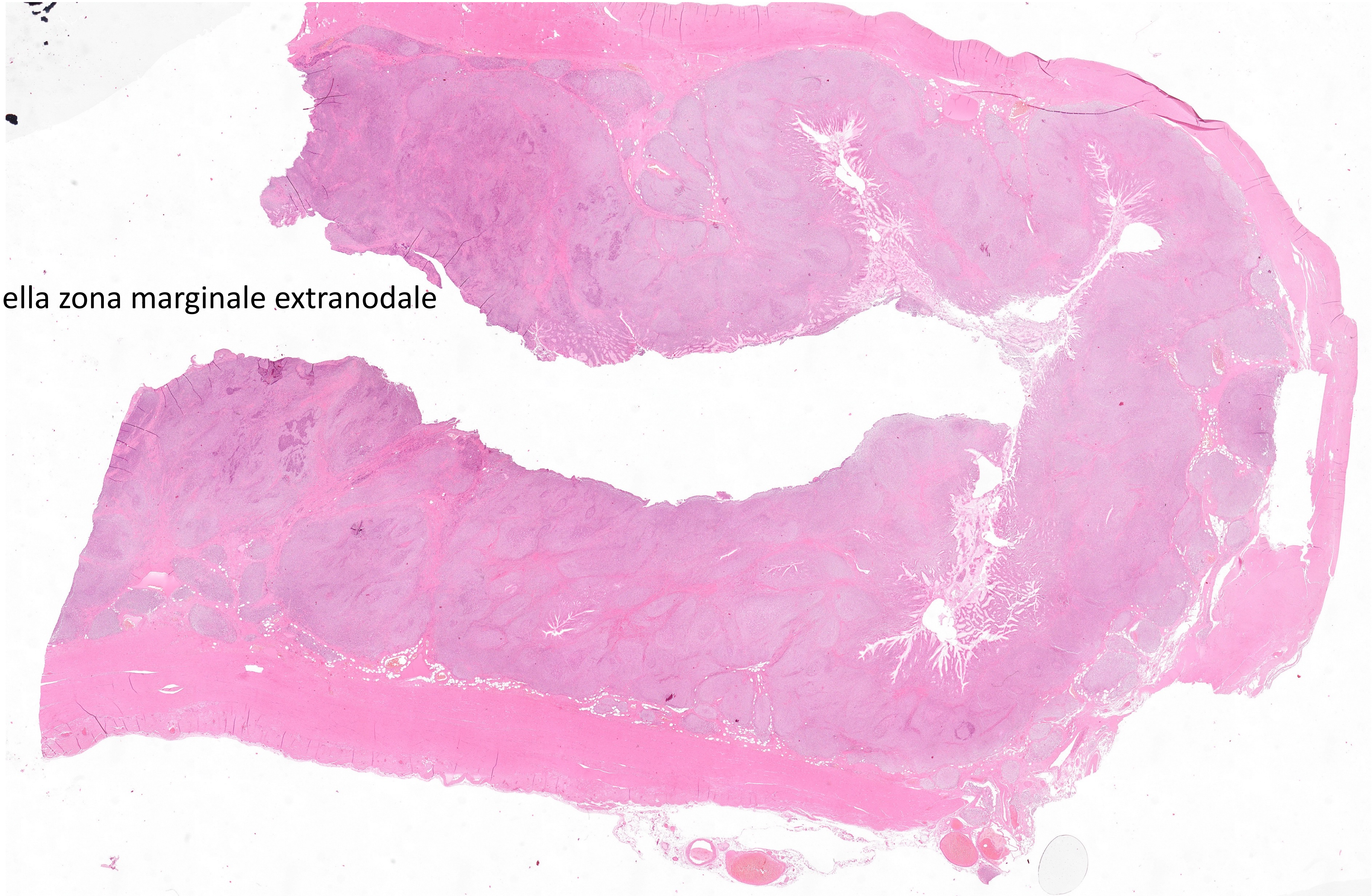
an indirect one, where chronic inflammation sustains and prolongs polyclonal proliferation of B-cells, with the consequent increased risk of double-stranded DNAbreaks and translocations owing to the inherent genetic instability of B-cells during somatic hypermutation and class switching recombination

Helicobacter pylori e linfomagenesi

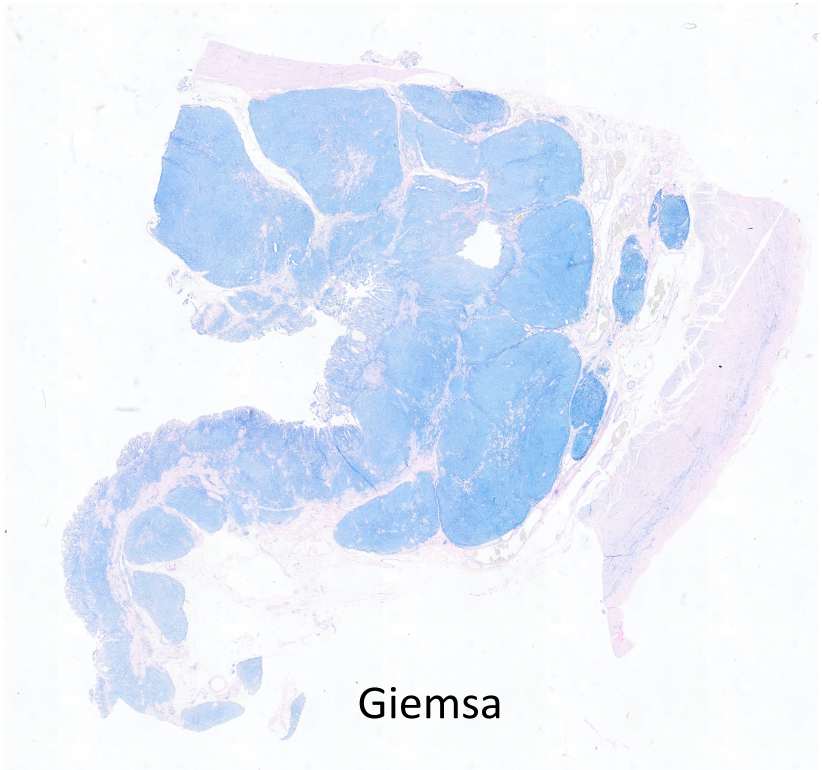

CagA
In B-lymphocytes
Tyrosine phosphorylation -dependent pathway
Tyrosine phosphorylation -independent pathway
In CagA-transgenic mice model
--
Developments of HP-associated GI and hematologic malignancies
SHP-2
ERK1/2
p38 MAPK
Bad-Ser112
Bcl-2
Bcl-xL
AKT1
HDM2
P53
IL-3 signaling
Functions G1 inhibitor
JAK/STAT
Anti-apoptosis
Proliferation

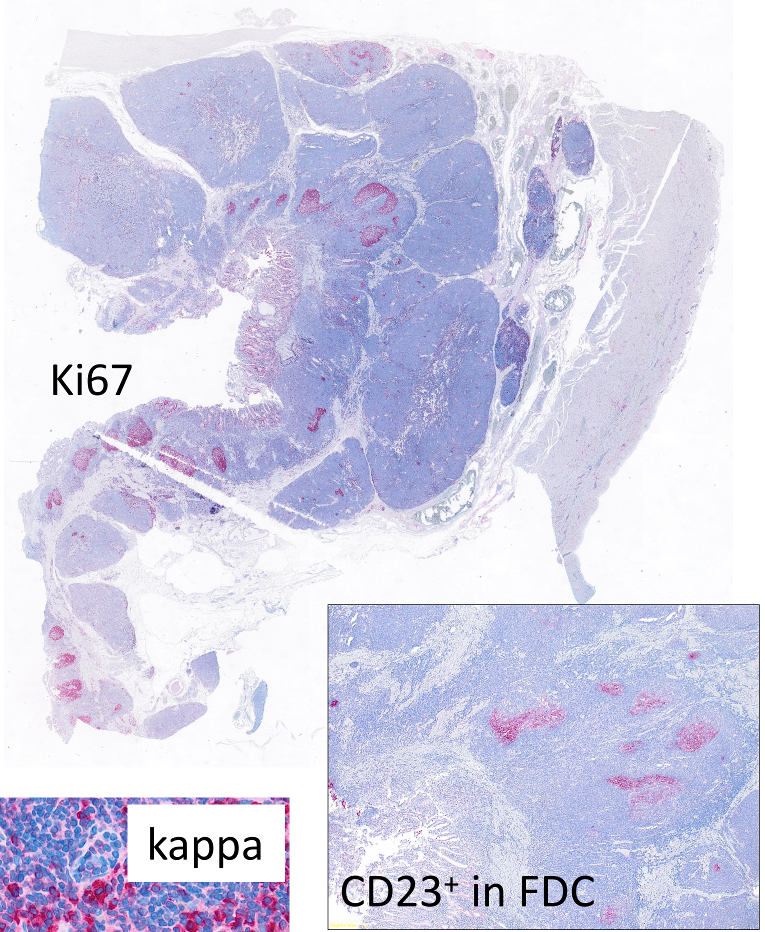
Kuo et al Cancers 2019

The cytotoxin-associated gene A (CagA) deregulates intracellular signaling pathways in B-lymphocytes in tyrosine phosphorylation-dependent and -independent manners to initiate the lymphomagenesis of Helicobacter pylori (HP)-dependent gastric mucosa-associated lymphoid tissue (MALT) lymphoma.

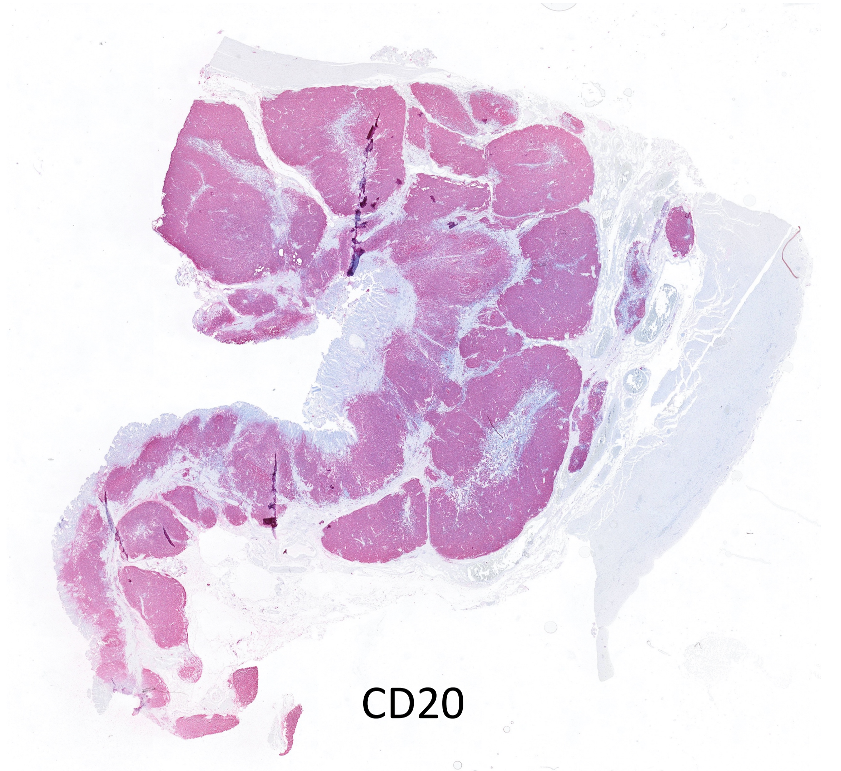


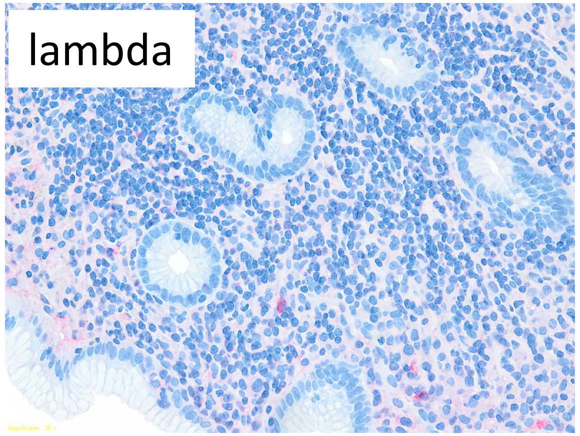
Linfoma della zona marginale extranodale

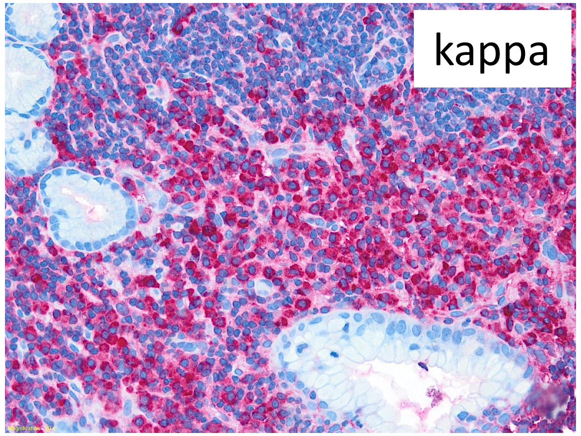

Giemsa


Ki67

CD23^{+} in FDC


CD20


lambda


kappa

Architettura:

multi-focalità,

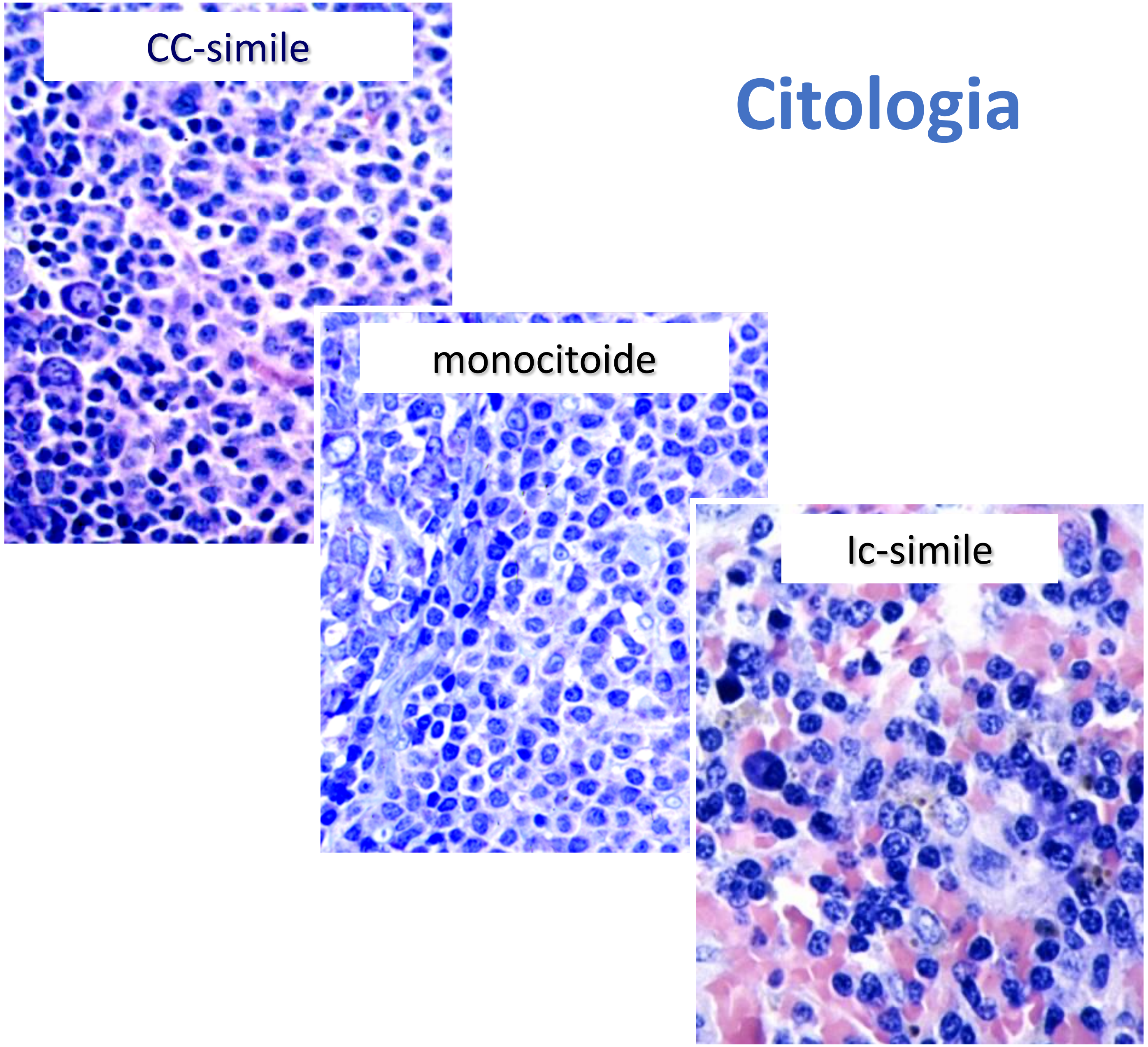
crescita:

perifollicolare

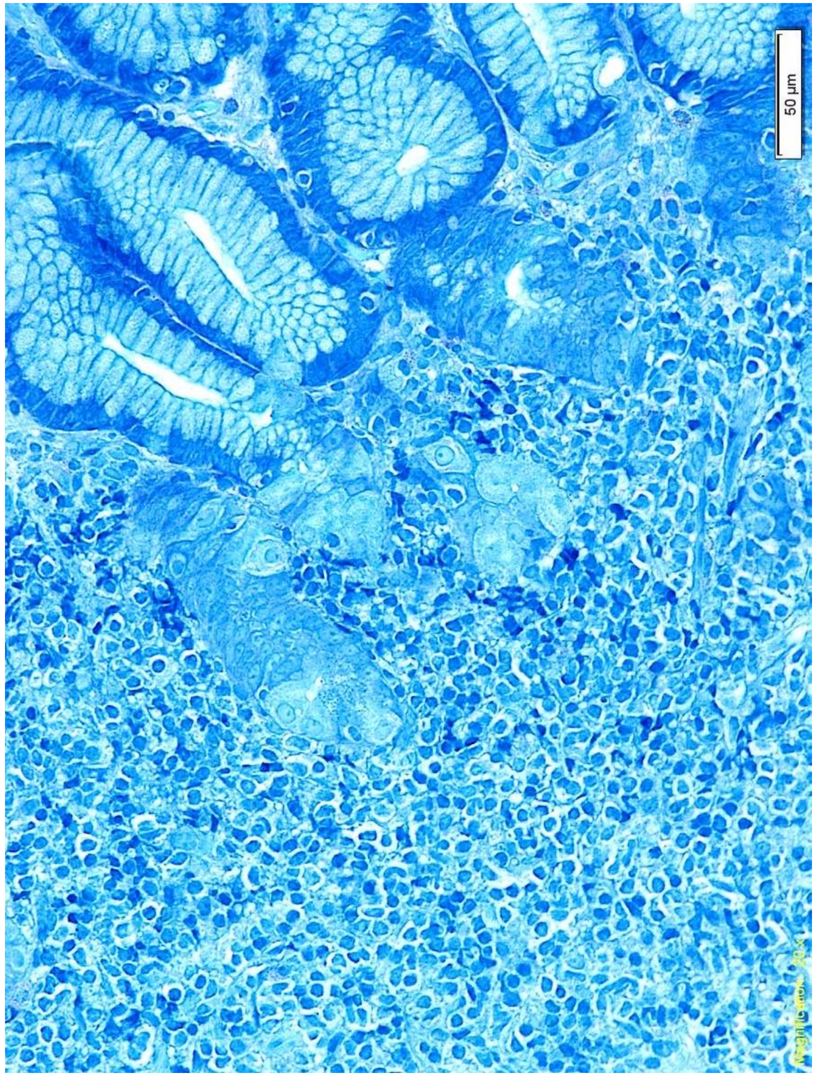
colonizzazione dei follicoli

diffusa

Citologia


CC-simile
monocitoide
lc-simile

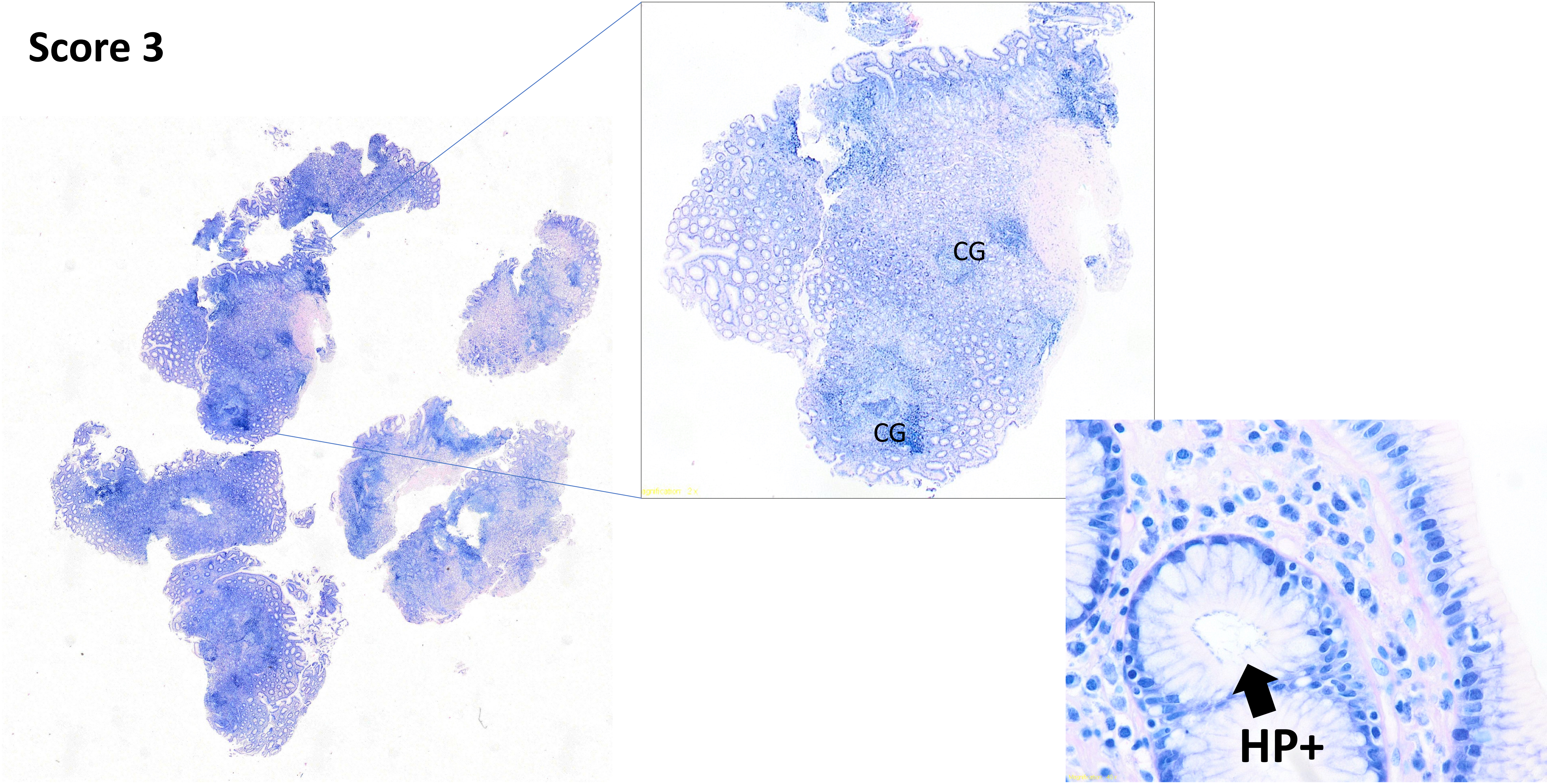
Lymphoepithelial Lesions (LEL)



Histology score to differentiate gastric MALT lymphoma from chronic gastritis

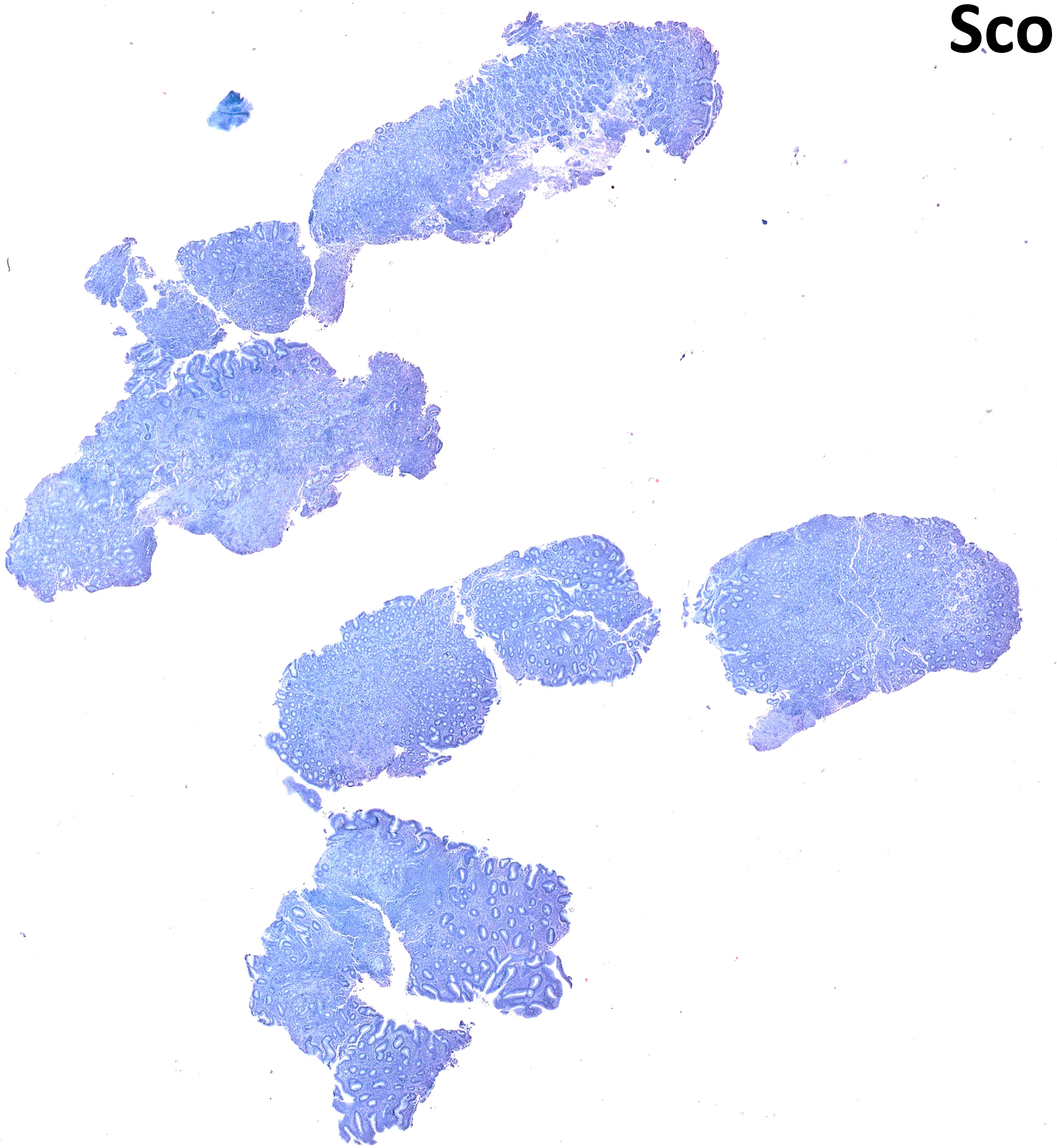
score	interpretation	histology
0	normal	occasional plasmacells
1	chronic active gastritis	lymphocyte clusters, no follicoles
2	follicular gastritis	prominent follicles, no lymphoepithelial lesions
3	suspicious, probably reactive	follicles, occasional adjacent lymphoepithelial lesions, no diffuse infiltrate
4	suspicious, probably lymphoma	follicles, diffuse margi al-zone cell infiltrate no lymphoepithelial lesions
5	MALT lymphoma	follicles, diffuse margi al-zone cell infiltrate lymphoepithelial lesions present

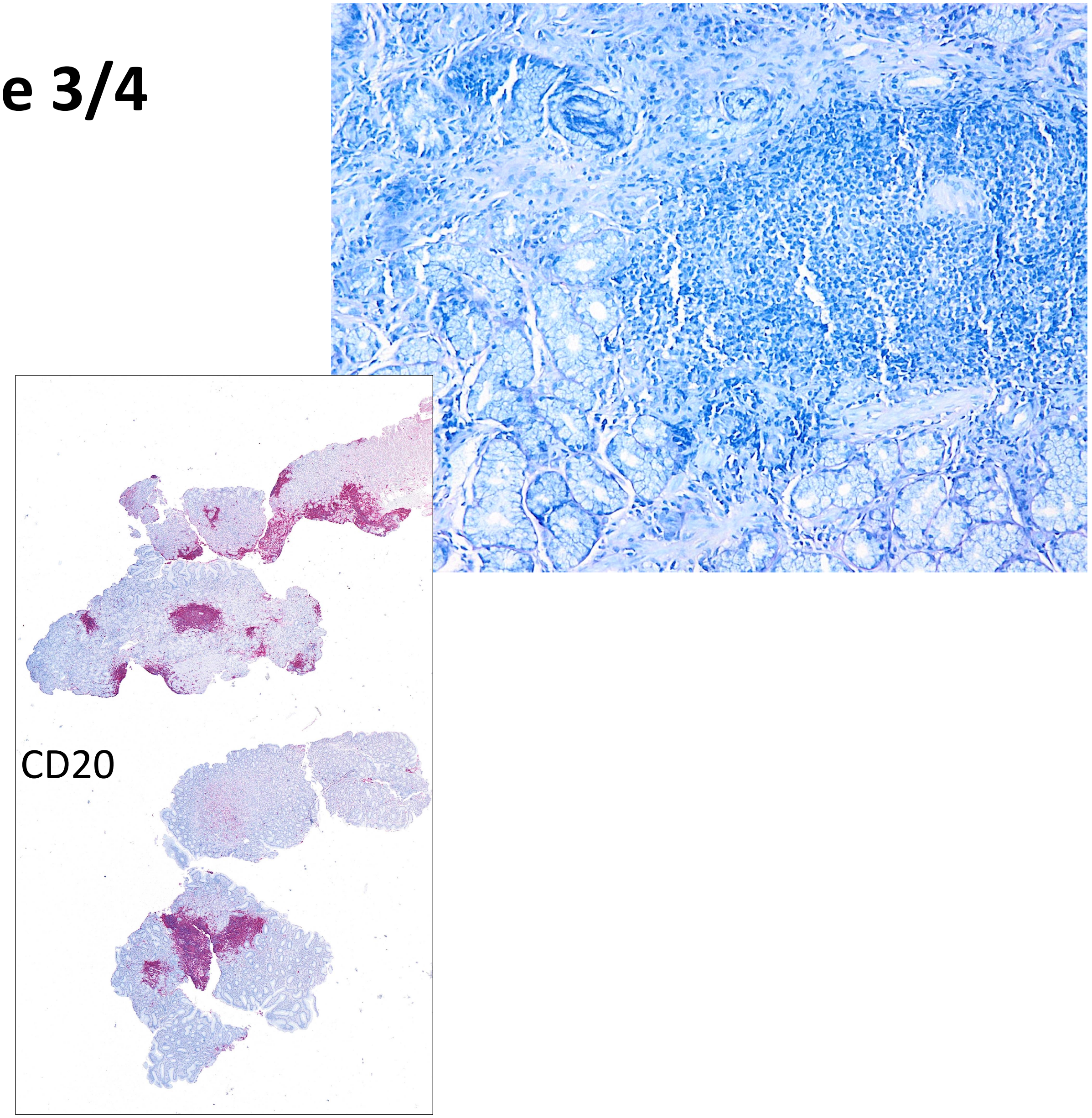
Score 3



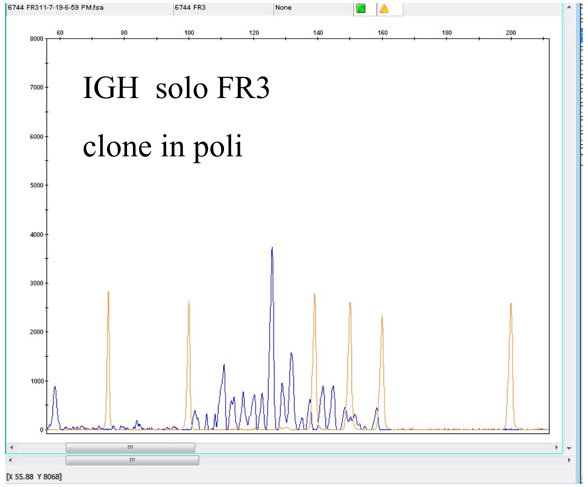
1° biopsia

Score 3/4



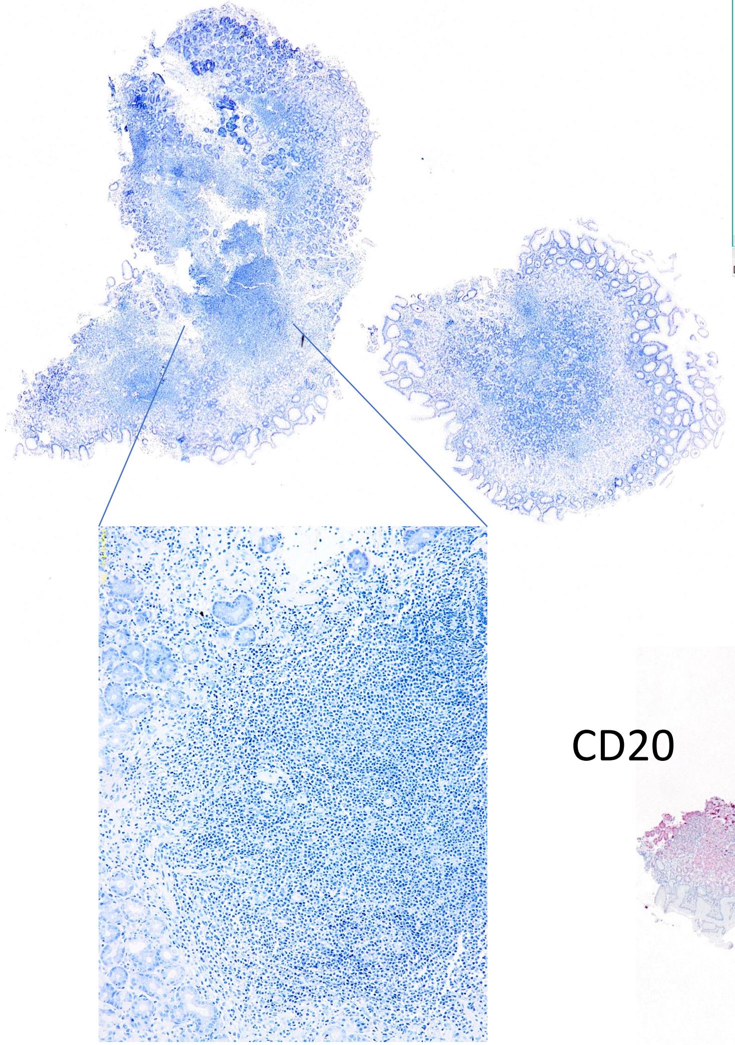


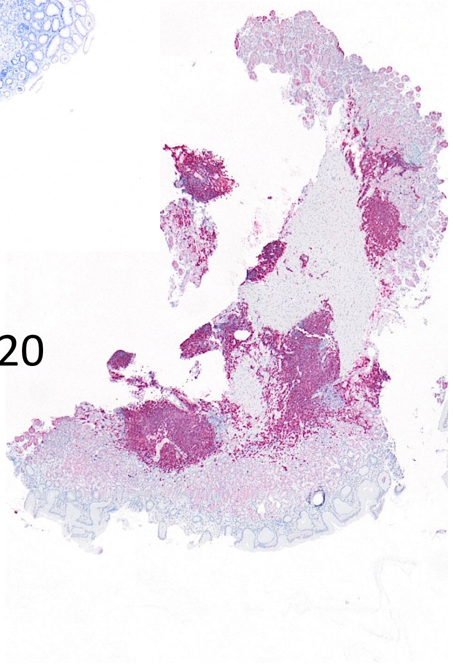
Score 5: linfoma MALT



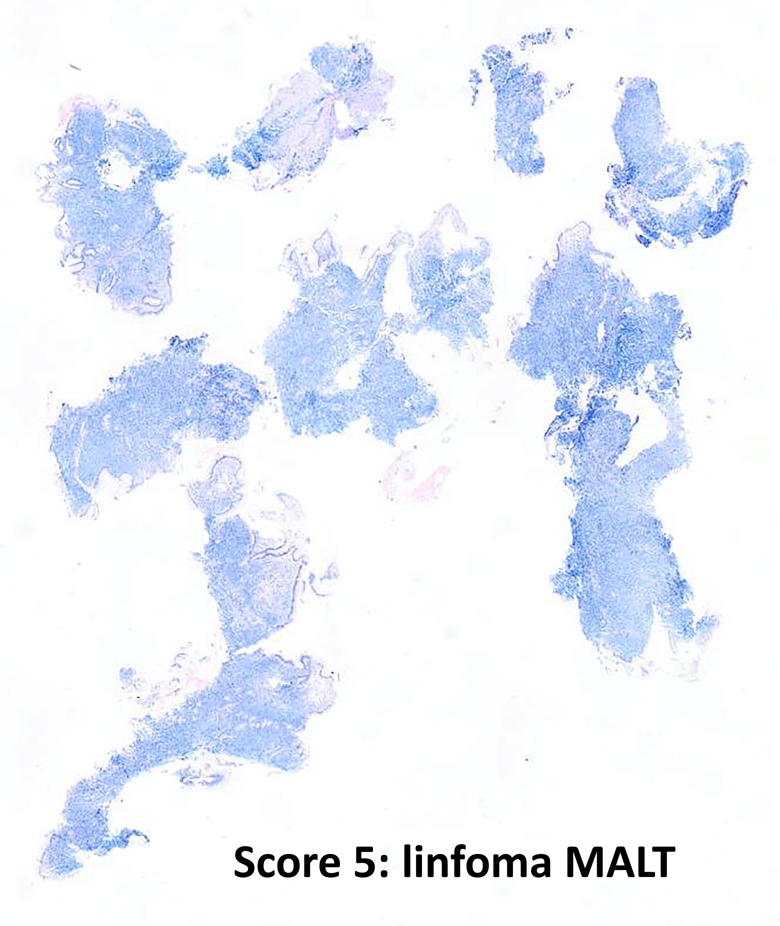
IGH solo FR3

clone in poli





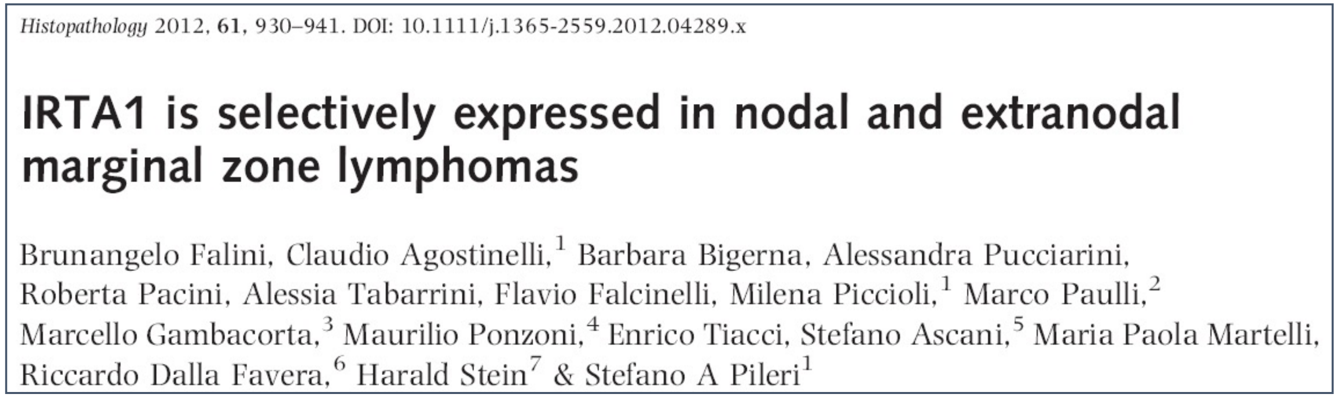
CD20



Score 5: linfoma MALT

Fenotipo di esclusione

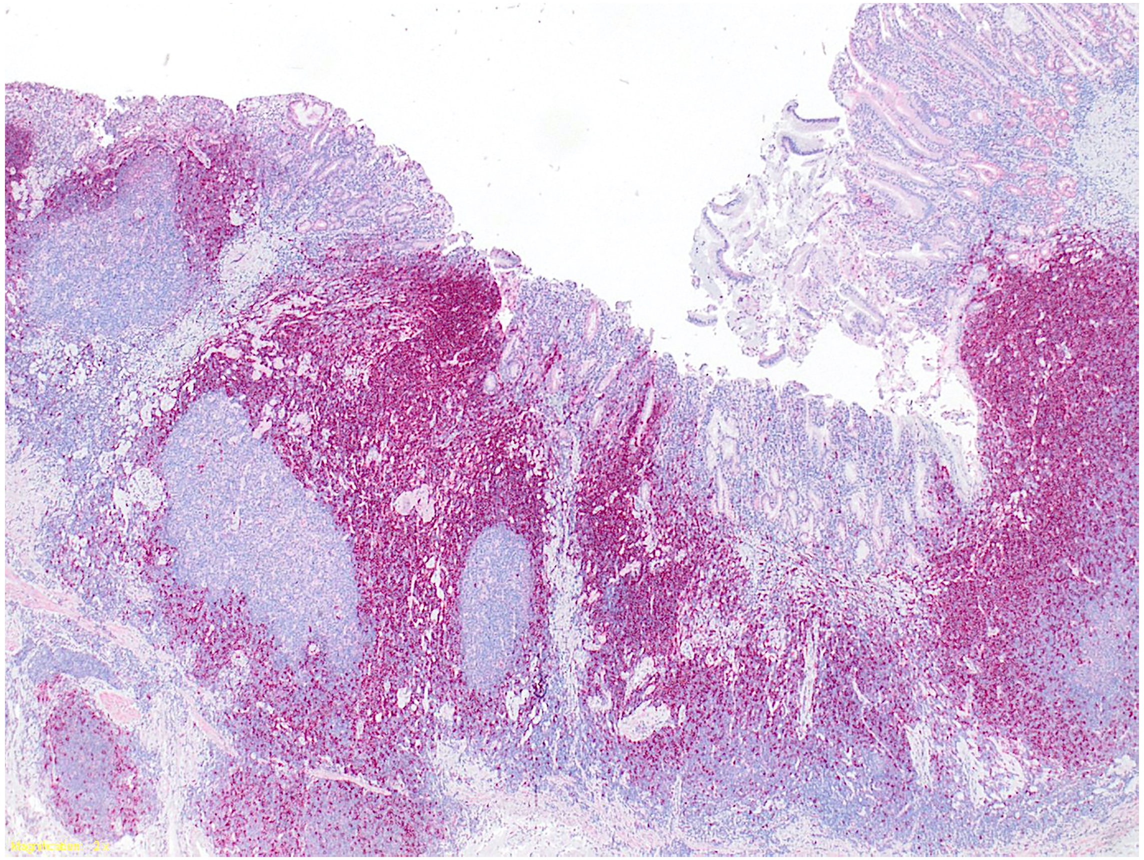
Follicolare	Mantellare	HCL	LLC
CD10+	CD5+	Annessina+	CD20 w+
BCL6+	Ciclina D1+	Ciclina D1+	CD5+
BCL2+	SOX11+	CD103+	CD23+
LMO2+		CD123+	LEF1+
HGAL+			IRF4 foc+



Histopathology 2012, **61**, 930–941. DOI: 10.1111/j.1365-2559.2012.04289.x

IRTA1 is selectively expressed in nodal and extranodal marginal zone lymphomas

Brunangelo Falini, Claudio Agostinelli,[1] Barbara Bigerna, Alessandra Pucciarini, Roberta Pacini, Alessia Tabarrini, Flavio Falcinelli, Milena Piccioli,[1] Marco Paulli,[2] Marcello Gambacorta,[3] Maurilio Ponzoni,[4] Enrico Tiacci, Stefano Ascani,[5] Maria Paola Martelli, Riccardo Dalla Favera,[6] Harald Stein[7] & Stefano A Pileri[1]



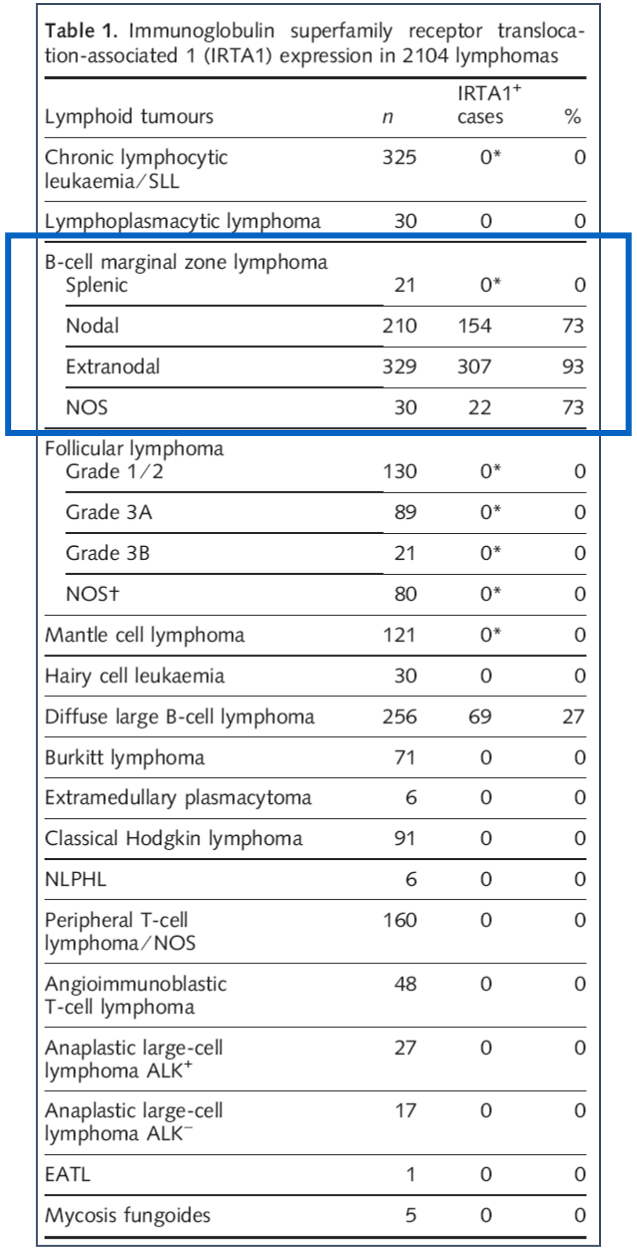
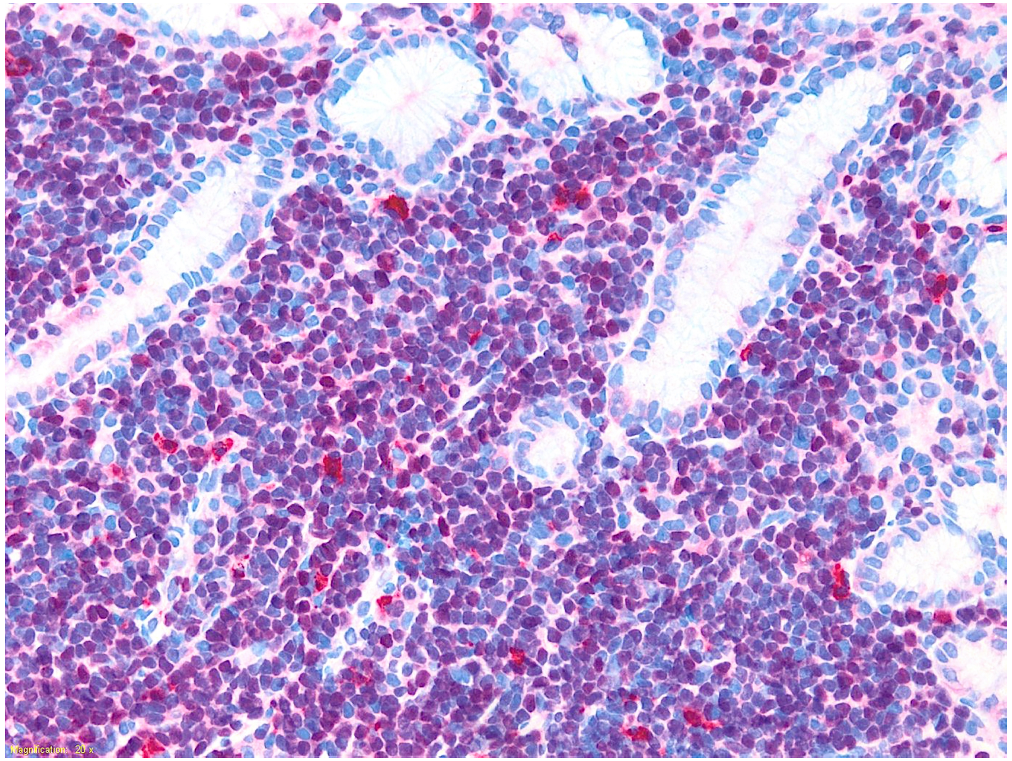
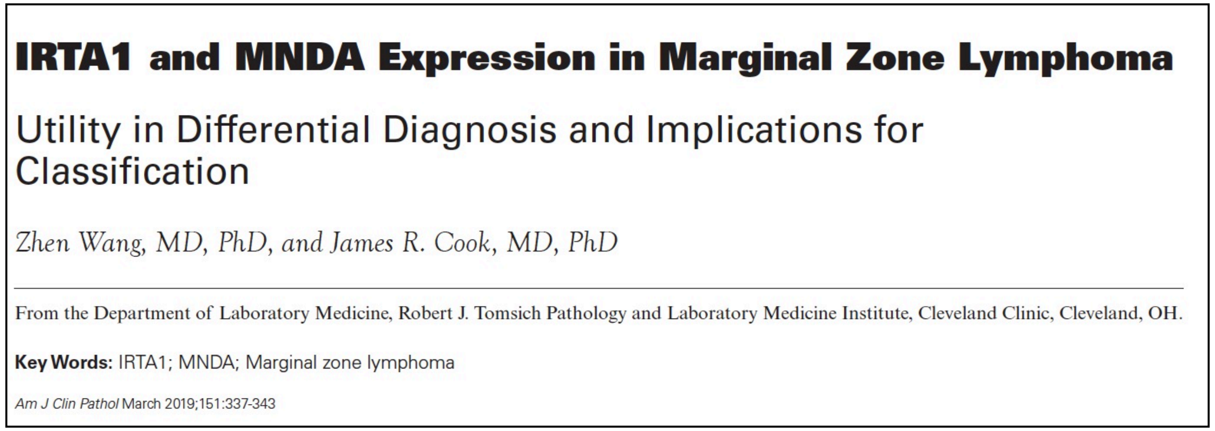


Table 1. Immunoglobulin superfamily receptor translocation-associated 1 (IRTA1) expression in 2104 lymphomas

Lymphoid tumours	*n*	IRTA1⁺ cases	%
Chronic lymphocytic leukaemia/SLL	325	0*	0
Lymphoplasmacytic lymphoma	30	0	0
B-cell marginal zone lymphoma			
Splenic	21	0*	0
Nodal	210	154	73
Extranodal	329	307	93
NOS	30	22	73
Follicular lymphoma			
Grade 1/2	130	0*	0
Grade 3A	89	0*	0
Grade 3B	21	0*	0
NOS†	80	0*	0
Mantle cell lymphoma	121	0*	0
Hairy cell leukaemia	30	0	0
Diffuse large B-cell lymphoma	256	69	27
Burkitt lymphoma	71	0	0
Extramedullary plasmacytoma	6	0	0
Classical Hodgkin lymphoma	91	0	0
NLPHL	6	0	0
Peripheral T-cell lymphoma/NOS	160	0	0
Angioimmunoblastic T-cell lymphoma	48	0	0
Anaplastic large-cell lymphoma ALK⁺	27	0	0
Anaplastic large-cell lymphoma ALK⁻	17	0	0
EATL	1	0	0
Mycosis fungoides	5	0	0

Myeloid Cell Nuclear Differentiation Antigen (MNDA)





IRTA1 and MNDA Expression in Marginal Zone Lymphoma

Utility in Differential Diagnosis and Implications for Classification

Zhen Wang, MD, PhD, and James R. Cook, MD, PhD

From the Department of Laboratory Medicine, Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH.

Key Words: IRTA1; MNDA; Marginal zone lymphoma

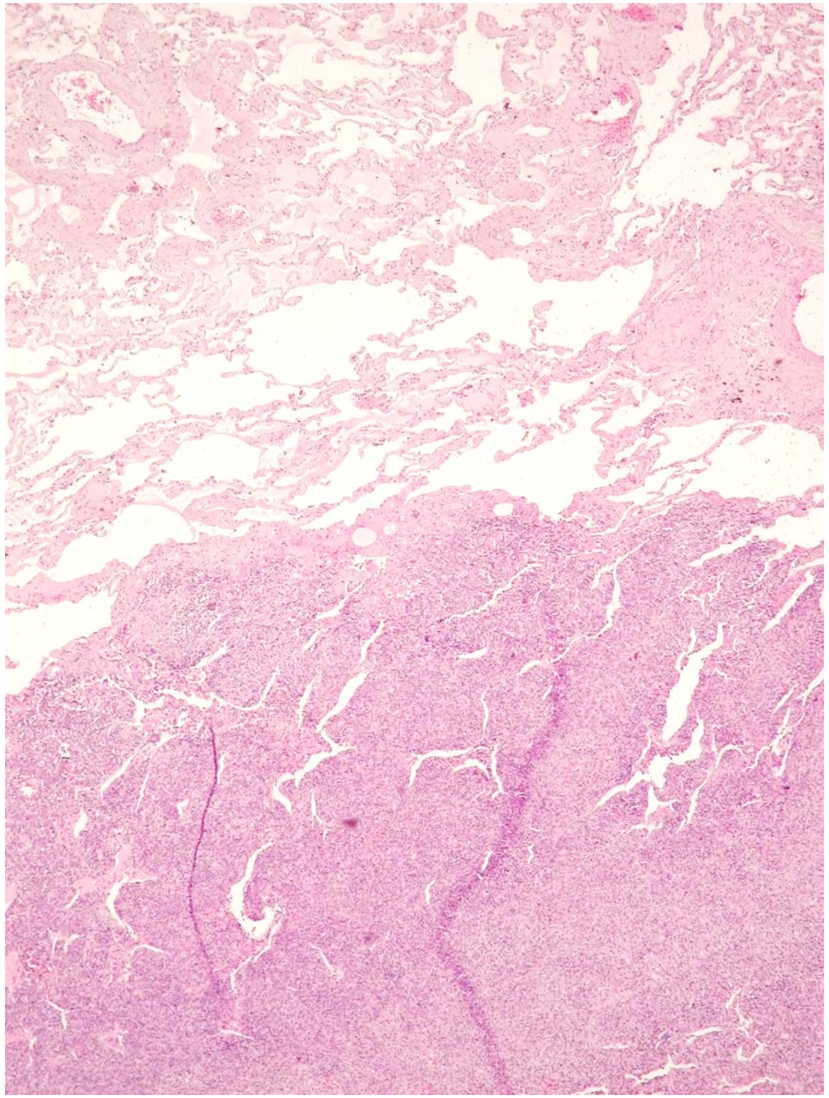
Am J Clin Pathol March 2019;151:337-343

Modalità di diffusione

- ENMZL gastrici tendono a localizzarsi in strutture mucose
- diffusione intragastrica e intestino (per interazione integrine α4β7 con HEV)
- 25% dei ENMZL gastrici hanno diffusione subclinica ad altre mucose (50% in ENMZL di altre sedi)
- la disseminazione secondaria allo stomaco è più rara

  in genere da ENMZL polmonari o intestinali (gastroscopia di staging)

ENMZL polmone



Profondità infiltrato:

mucosa/sottomucosa = regr.$^{+}$

muscolare propria = regr.$^{-}$

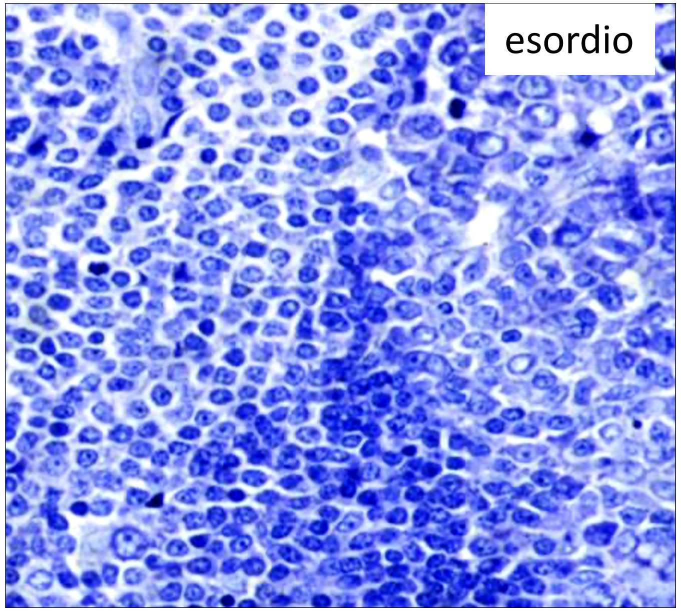
eco-endoscopia.

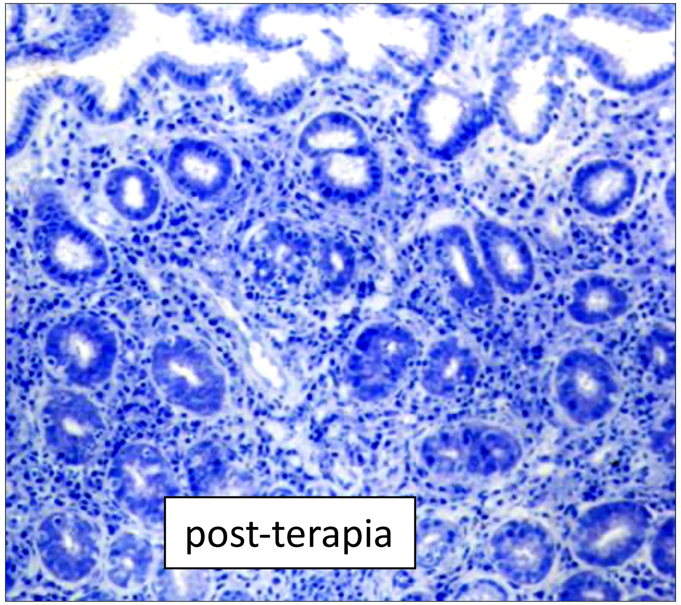
Valutazione regressione:

istologia (più attendibile di PCR);

tempo richiesto: 2-28 mesi.

La regressione può essere rapida (4 mesi) ma in buona parte dei casi può ritardare fino a d 1 o > anni


esordio


post-terapia

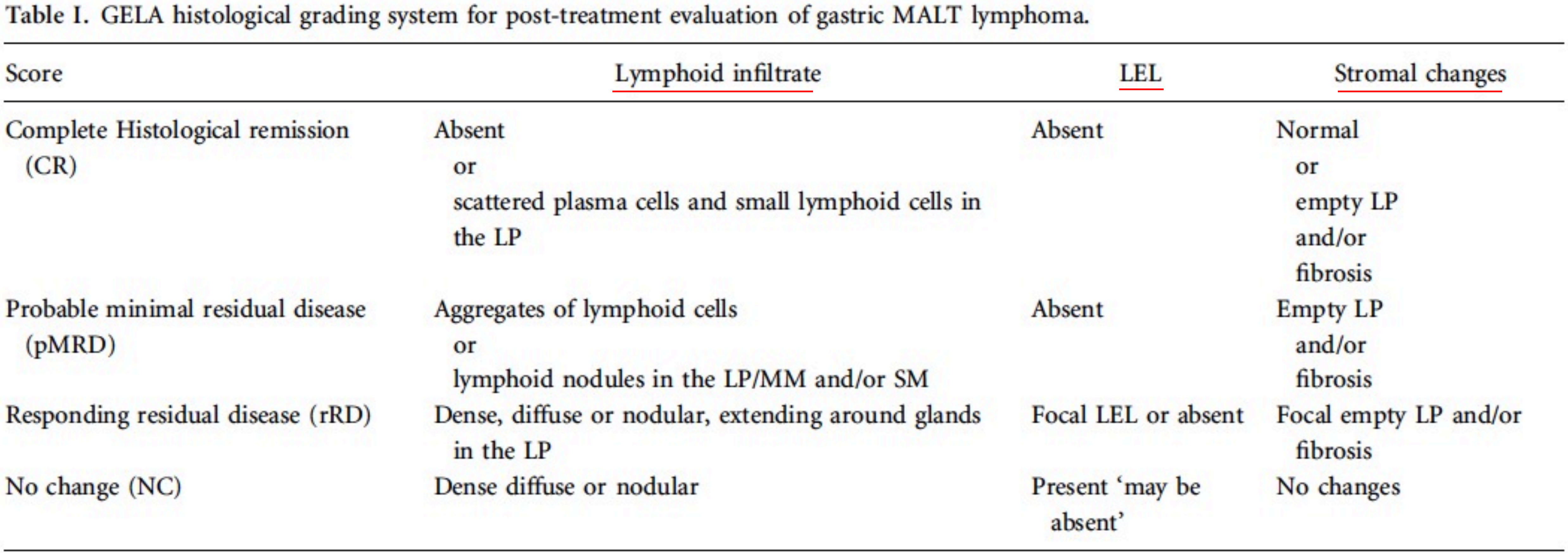
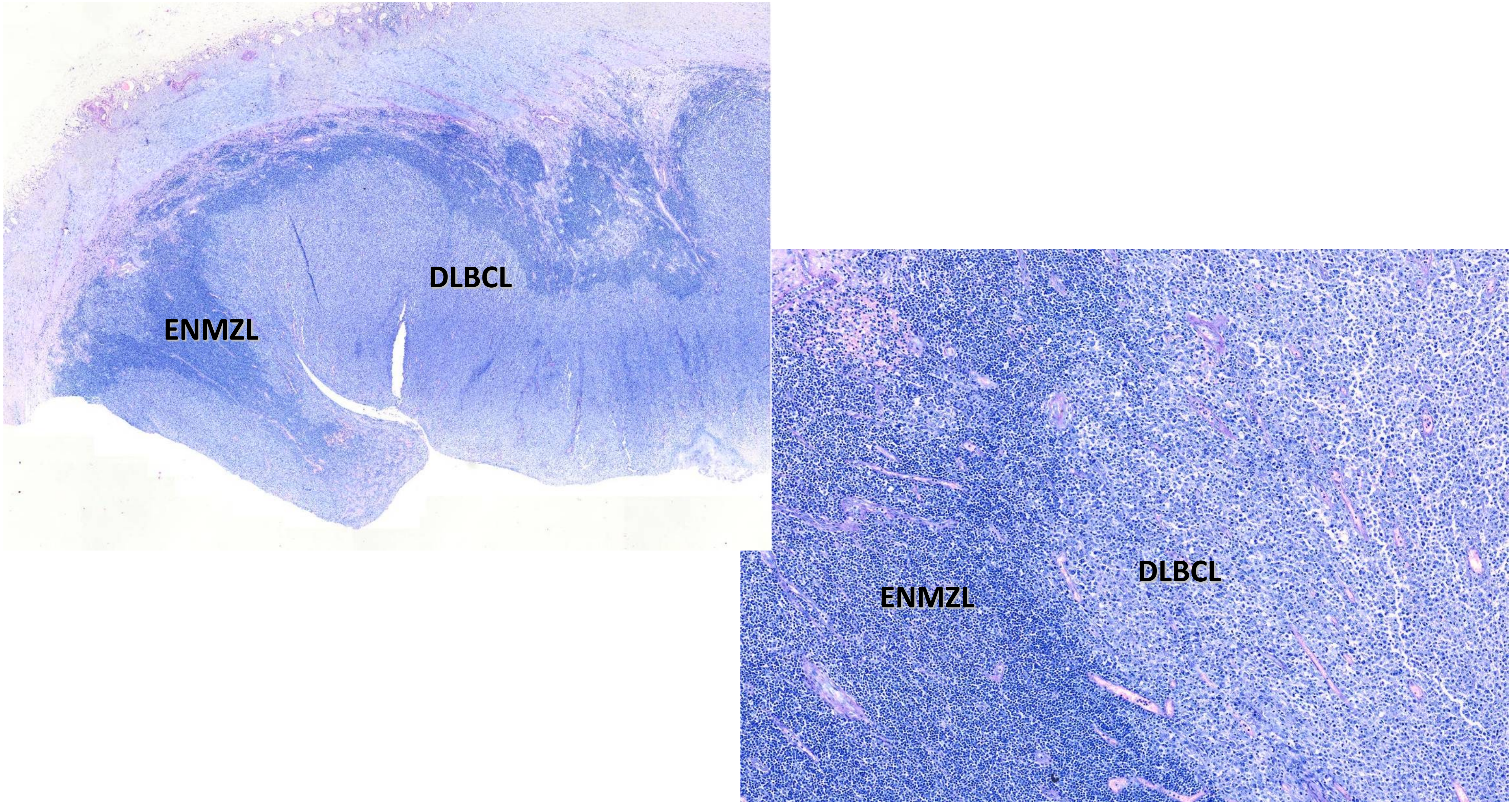


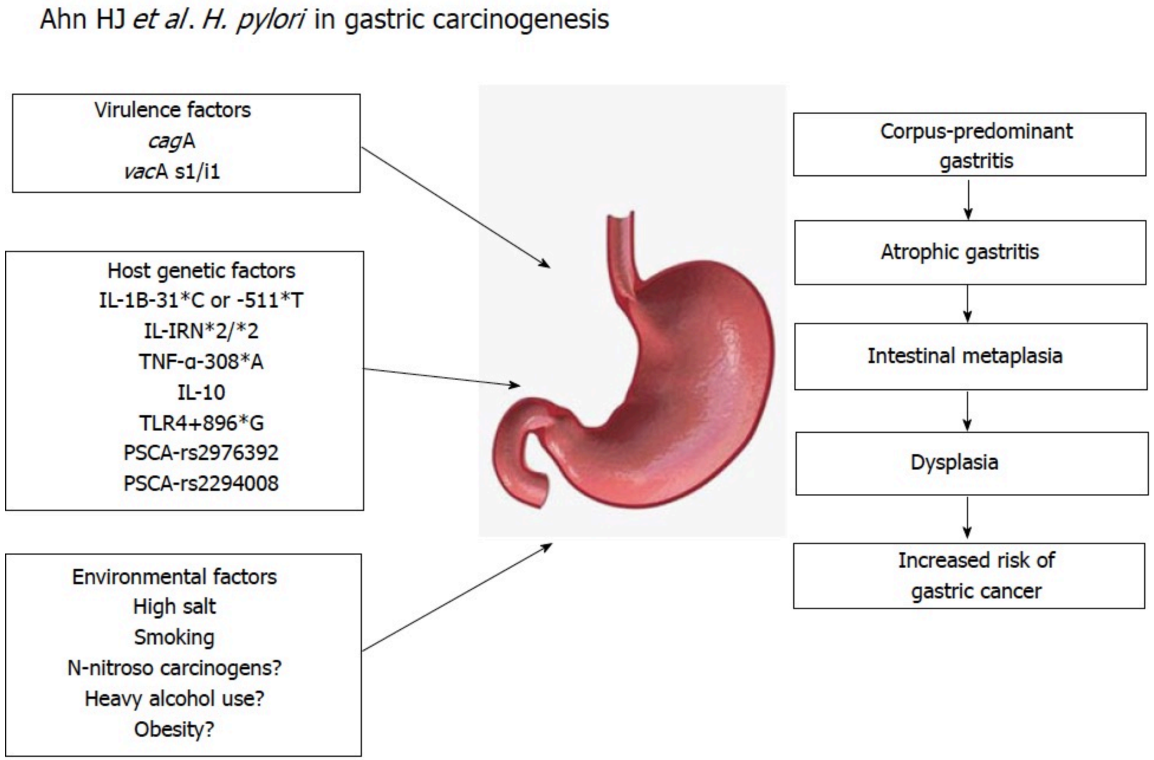
Table I. GELA histological grading system for post-treatment evaluation of gastric MALT lymphoma.

Score	Lymphoid infiltrate	LEL	Stromal changes
Complete Histological remission (CR)	Absent or scattered plasma cells and small lymphoid cells in the LP	Absent	Normal or empty LP and/or fibrosis
Probable minimal residual disease (pMRD)	Aggregates of lymphoid cells or lymphoid nodules in the LP/MM and/or SM	Absent	Empty LP and/or fibrosis
Responding residual disease (rRD)	Dense, diffuse or nodular, extending around glands in the LP	Focal LEL or absent	Focal empty LP and/or fibrosis
No change (NC)	Dense diffuse or nodular	Present 'may be absent'	No changes


DLBCL
ENMZL
DLBCL
ENMZL

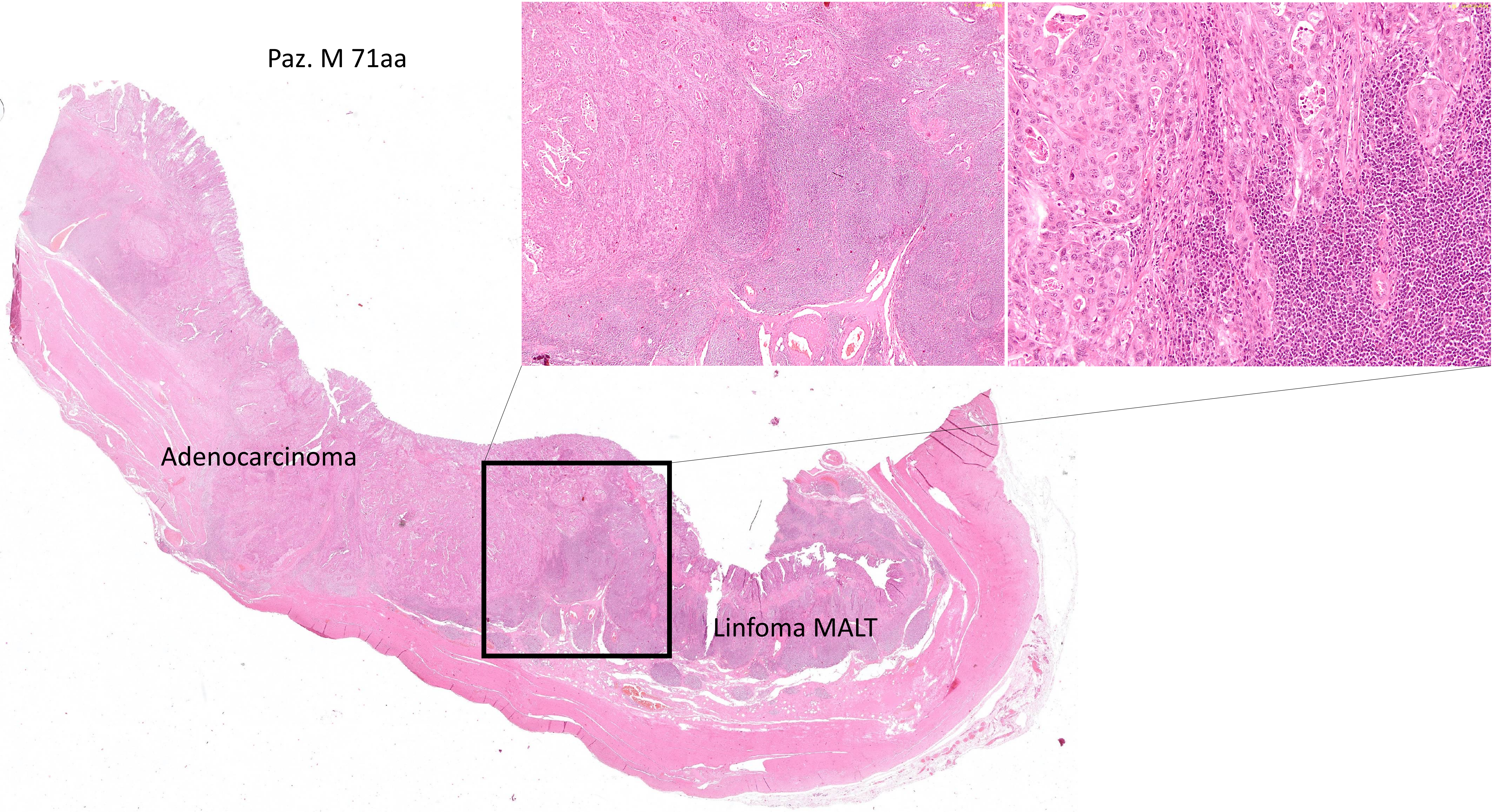
In follow-up:

- HP è carcinogeno di classe I (IARC)
  per il carcinoma gastrico
- pazienti con G-ENMZL sono a maggior rischio
  di carcinomi gastrici metacroni
- riscontro di metaplasia intestinale in 50-70%
  dei pazienti a 6-18 mesi dalla diagnosi con G-EMZL
- Per quanto tempo mantenere follow-up?
  (rischio di recidive tardive di linfoma
  e rischio sviluppo carcinoma)


Ahn HJ *et al*. *H. pylori* in gastric carcinogenesis
Virulence factors
*cag*A
*vac*A s1/i1
Host genetic factors
IL-1B-31*C or -511*T
IL-IRN*2/*2
TNF-α-308*A
IL-10
TLR4+896*G
PSCA-rs2976392
PSCA-rs2294008
Environmental factors
High salt
Smoking
N-nitroso carcinogens?
Heavy alcohol use?
Obesity?
Corpus-predominant gastritis
Atrophic gastritis
Intestinal metaplasia
Dysplasia
Increased risk of gastric cancer

World J Gatroenterology 2015

Paz. M 71aa


Adenocarcinoma
Linfoma MALT

ENMZL: alterazioni genomiche numeriche e strutturali

Gains / Losses (20-40%, > che in altri linfomi):

+18/18q ricorrente

+3/3q ricorrente

del 6q23.3 (nel 15-30% TNFAIP3/A20)

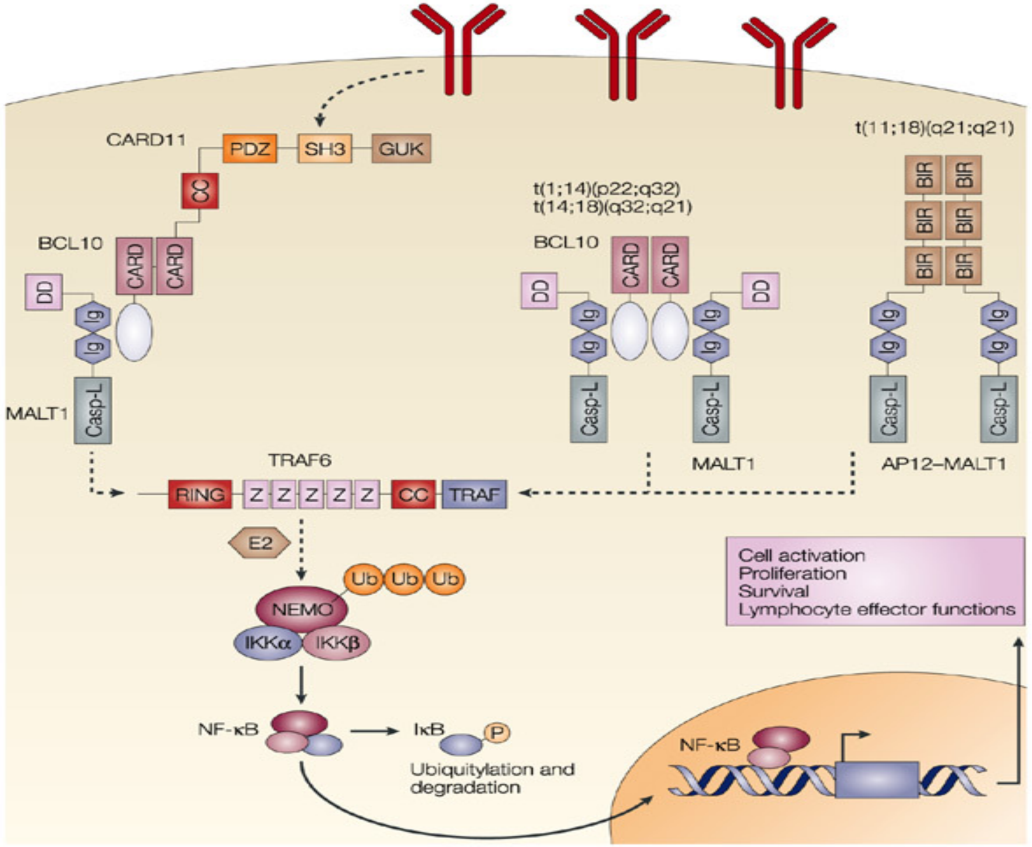
Traslocazioni:

t(11;18)(q21;q21) *BIRC3/MALT1*

t(1;14)(p22;q32) *IGH/BCL10*

t(14;18)(q32;q21) *IGH/MALT1*

t(3:14)(p13;q32) *IGH/FOXP1*

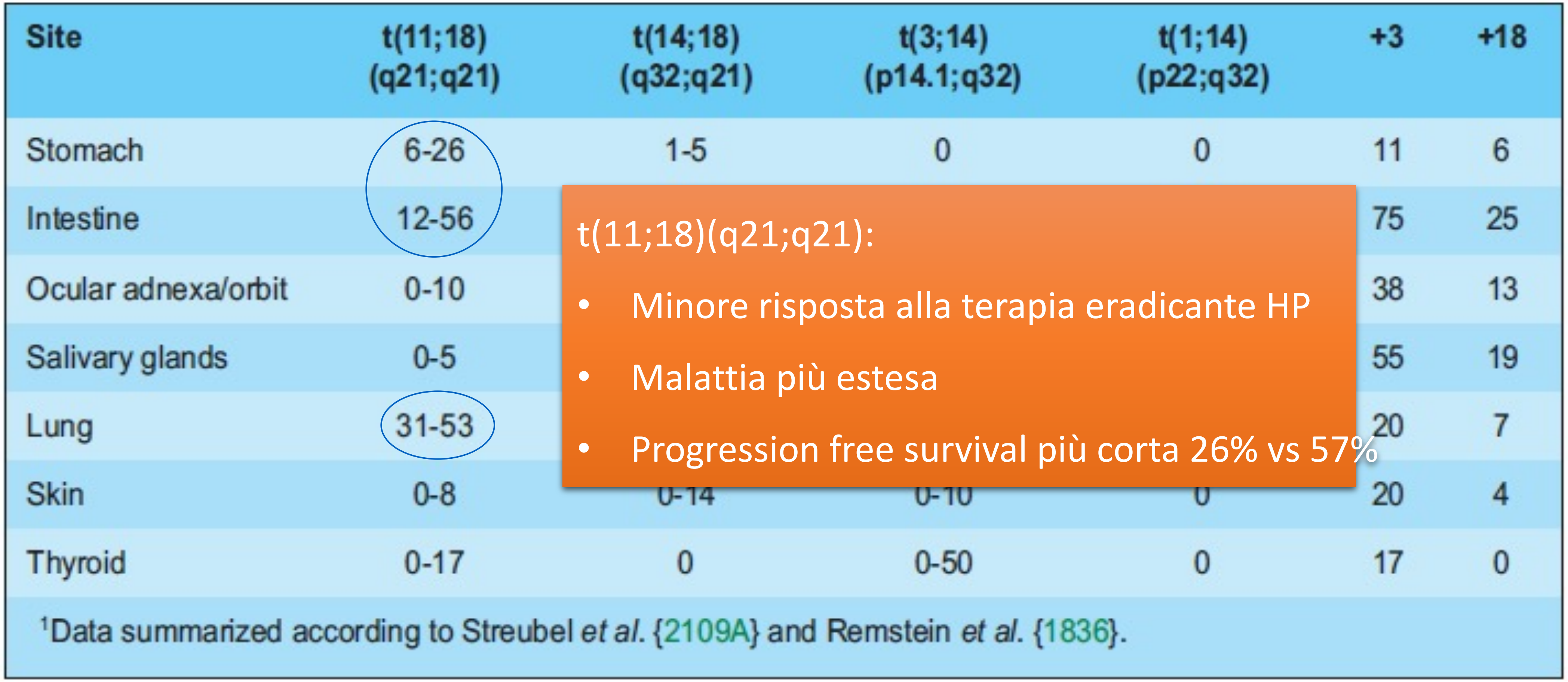


CARD11
PDZ
SH3
GUK
CC
BCL10
CARD
CARD
DD
Ig
Ig
MALT1
Casp-L
t(1;14)(p22;q32)
t(14;18)(q32;q21)
BCL10
CARD
CARD
DD
Ig
Ig
Casp-L
DD
Ig
Ig
Casp-L
MALT1
t(11;18)(q21;q21)
BIR
BIR
BIR
BIR
BIR
BIR
Ig
Ig
Casp-L
Ig
Ig
Casp-L
AP12–MALT1
TRAF6
RING
Z
Z
Z
Z
Z
CC
TRAF
E2
Ub
Ub
Ub
NEMO
IKKα
IKKβ
NF-κB
IκB
P
Ubiquitylation and degradation
NF-κB
Cell activation
Proliferation
Survival
Lymphocyte effector functions

(Isaacson, Nat Rev Cancer 2004; 4:644-53)

Nature Reviews | Cancer

Frequenza diversa in base alla sede



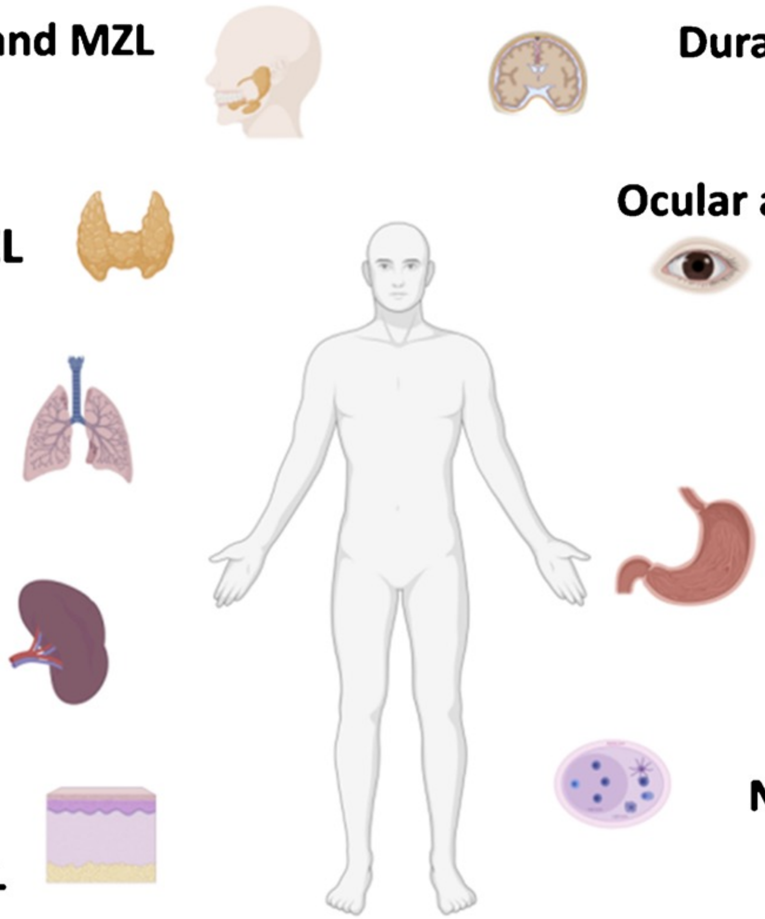
Site	t(11;18) (q21;q21)	t(14;18) (q32;q21)	t(3;14) (p14.1;q32)	t(1;14) (p22;q32)	+3	+18
Stomach	6-26	1-5	0	0	11	6
Intestine	12-56	[illegible]	[illegible]	[illegible]	75	25
Ocular adnexa/orbit	0-10	[illegible]	[illegible]	[illegible]	38	13
Salivary glands	0-5	[illegible]	[illegible]	[illegible]	55	19
Lung	31-53	[illegible]	[illegible]	[illegible]	20	7
Skin	0-8	0-14	0-10	0	20	4
Thyroid	0-17	0	0-50	0	17	0

[1] Data summarized according to Streubel *et al.* {2109A} and Remstein *et al.* {1836}.

t(11;18)(q21;q21):

- Minore risposta alla terapia eradicante HP
- Malattia più estesa
- Progression free survival più corta 26% vs 57%

Certain translocations are associated with particular sites of origin (WHO 2008)



Salivary gland MZL

TBL1XR1	24%
GPR34	16%
NOTCH2	11%
SPEN	11%
KMT2C	11%

Thyroid MZL

TET2	65%
TNFRSF14	44%
PIK3CD	23%
CCR6	8%
FOXO1	8%

Pulmonary MZL

KMT2D	25%
TNFAIP3	18%
PRDM1	12%
NOTCH1	12%
EP300	11%

Splenic MZL

KLF2	18%
NOTCH2	16%
TP53	12%
TNFAIP3	8%
KMT2D	7%

Cutaneous MZL

FAS	63%
SLAMF1	24%
SPEN	18%
NCOR2	13%
CASP10	11%

Dural MZL

TNFAIP3	45%
NOTCH2	36%
TLBXR1	36%
EP300	18%
KLHL6	18%

Ocular adnexal MZL

TNFAIP3	32%
KMT2D	15%
KMT2C	11%
LRP1B	11%
MYD88	10%

Gastric MZL

NOTCH1	16%
TNFAIP3	15%
NF1	14%
TRAF3	13%
TET2	11%

Nodal MZL

KMT2D	20%
TNFAIP3	14%
CREBBP	12%
PTPRD	12%
KLF2	12%

Vela et al Virchows Archive 2021

EMZL gastrico H. pylori negativo

- Aumento dei casi di ENMZL gastrici HP- in ultimi 20 aa:

  da 5%-10% a 30-50%
- La persistenza della flogosi cronica può portare a scomparsa istologia

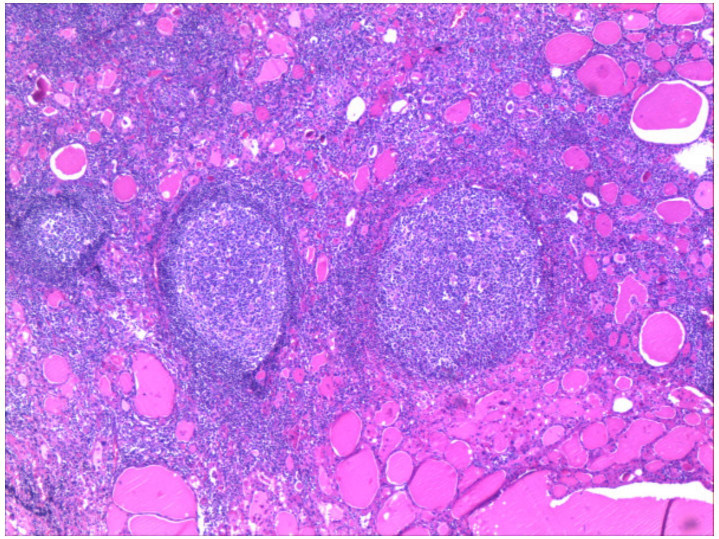
  di HP ma breath-test, sierologia e test feci+
- Spiegazioni:

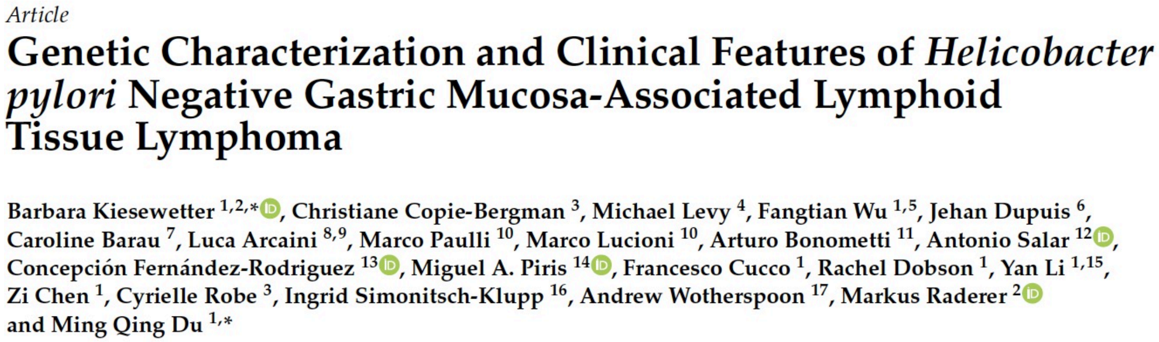
  test falsi negativi

  infezioni da altri batteri (*H. heilmannii, H. suis, H.bizzozzeri, salomnois*)?

  associazione con malattie autoimmuni (tiroiditi di Hashimoto)?

Tessuto MALT in tiroidite di Hashimoto





Article

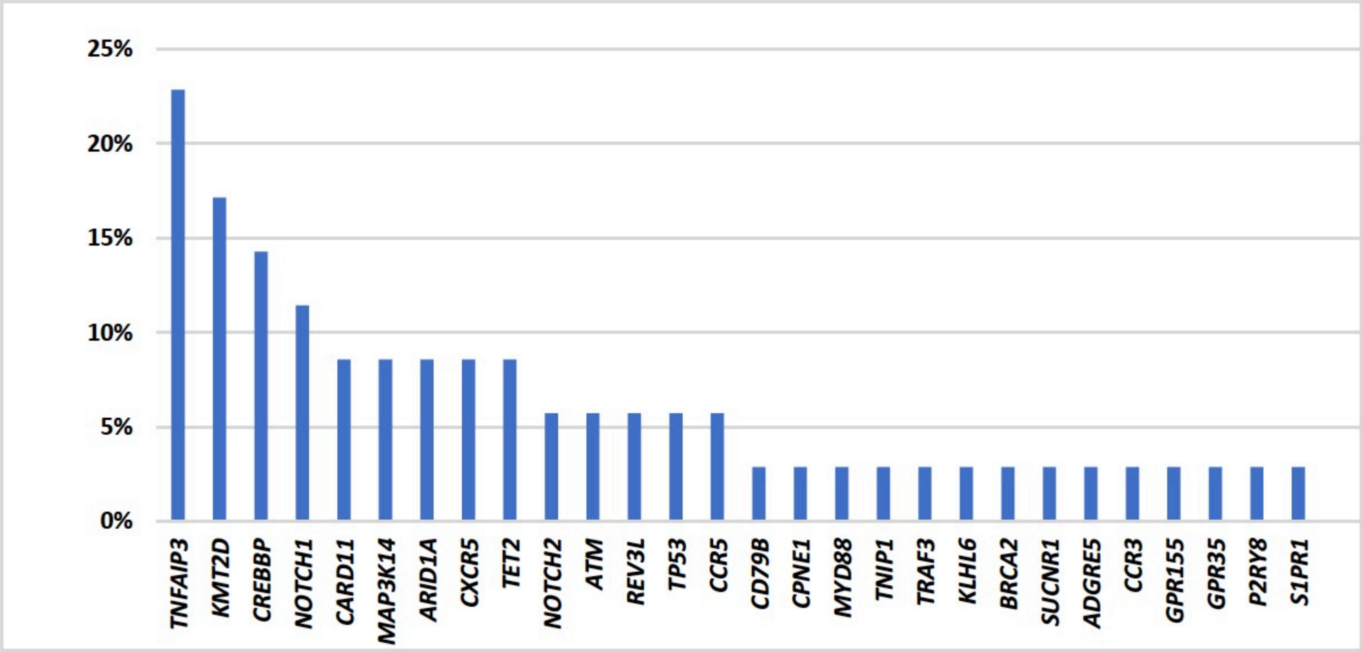
Genetic Characterization and Clinical Features of *Helicobacter pylori* Negative Gastric Mucosa-Associated Lymphoid Tissue Lymphoma

Barbara Kiesewetter [1,2,*], Christiane Copie-Bergman [3], Michael Levy [4], Fangtian Wu [1,5], Jehan Dupuis [6], Caroline Barau [7], Luca Arcaini [8,9], Marco Paulli [10], Marco Lucioni [10], Arturo Bonometti [11], Antonio Salar [12], Concepción Fernández-Rodriguez [13], Miguel A. Piris [14], Francesco Cucco [1], Rachel Dobson [1], Yan Li [1,15], Zi Chen [1], Cyrielle Robe [3], Ingrid Simonitsch-Klupp [16], Andrew Wotherspoon [17], Markus Raderer [2] and Ming Qing Du [1,*]

In G-ENMZL HP- :

t(11;18)(q21;q21)

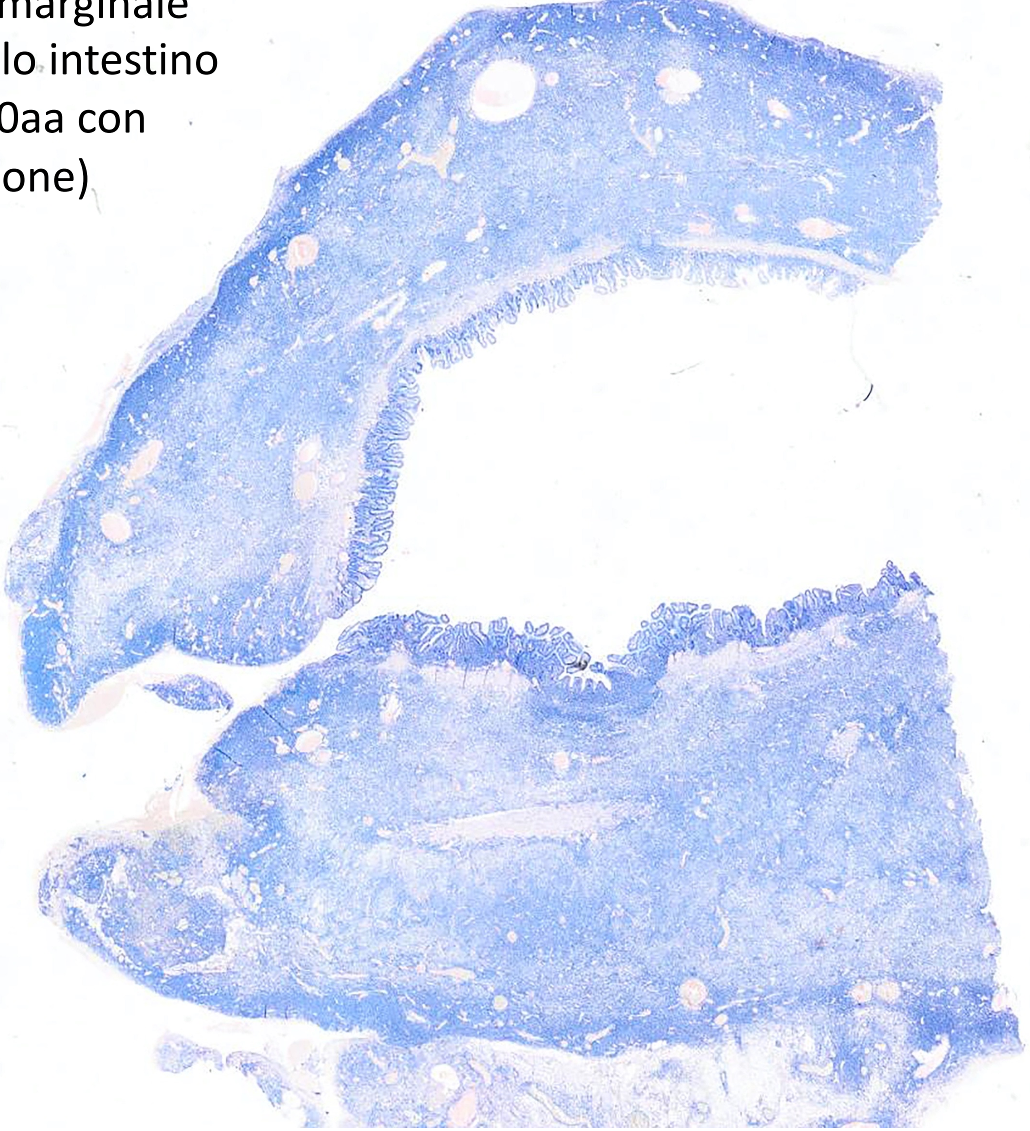
e iper-espressione BCL10

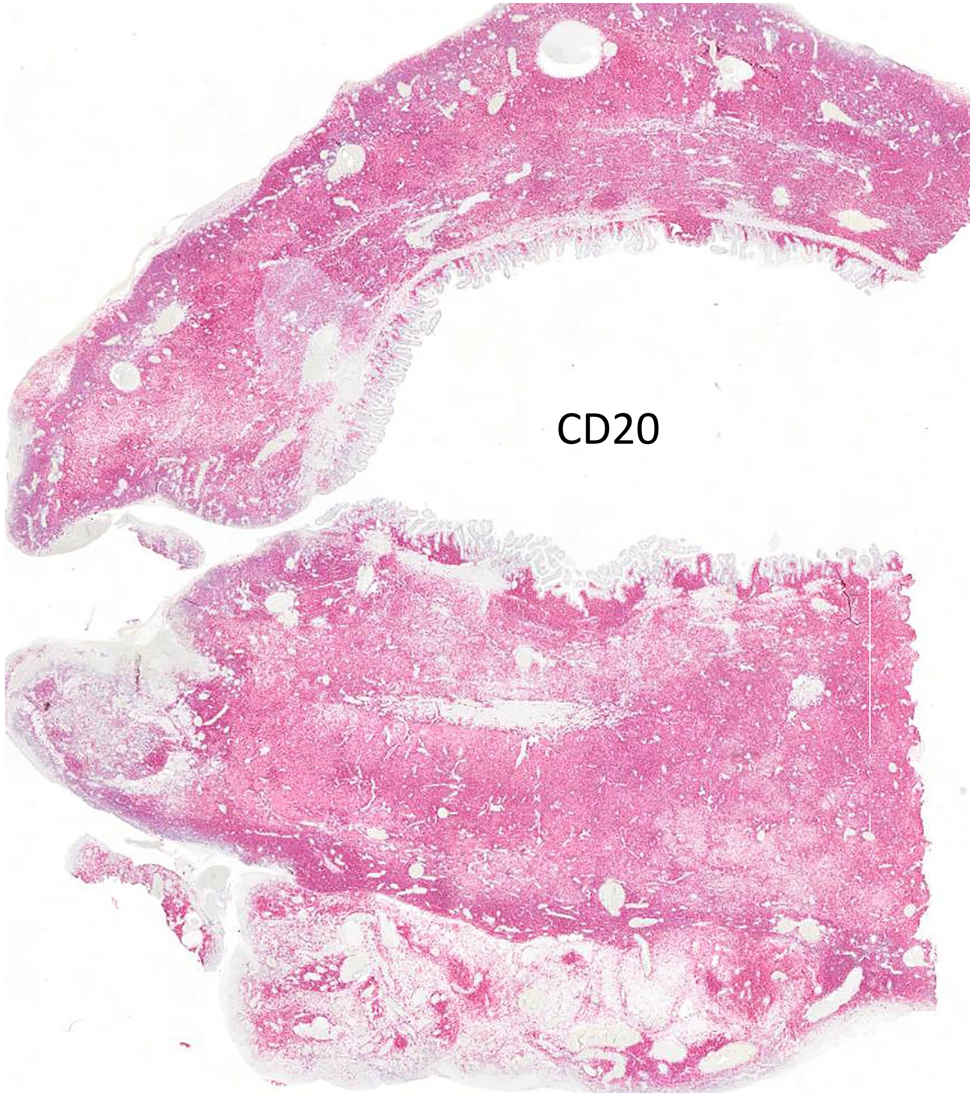


Cancers 2021

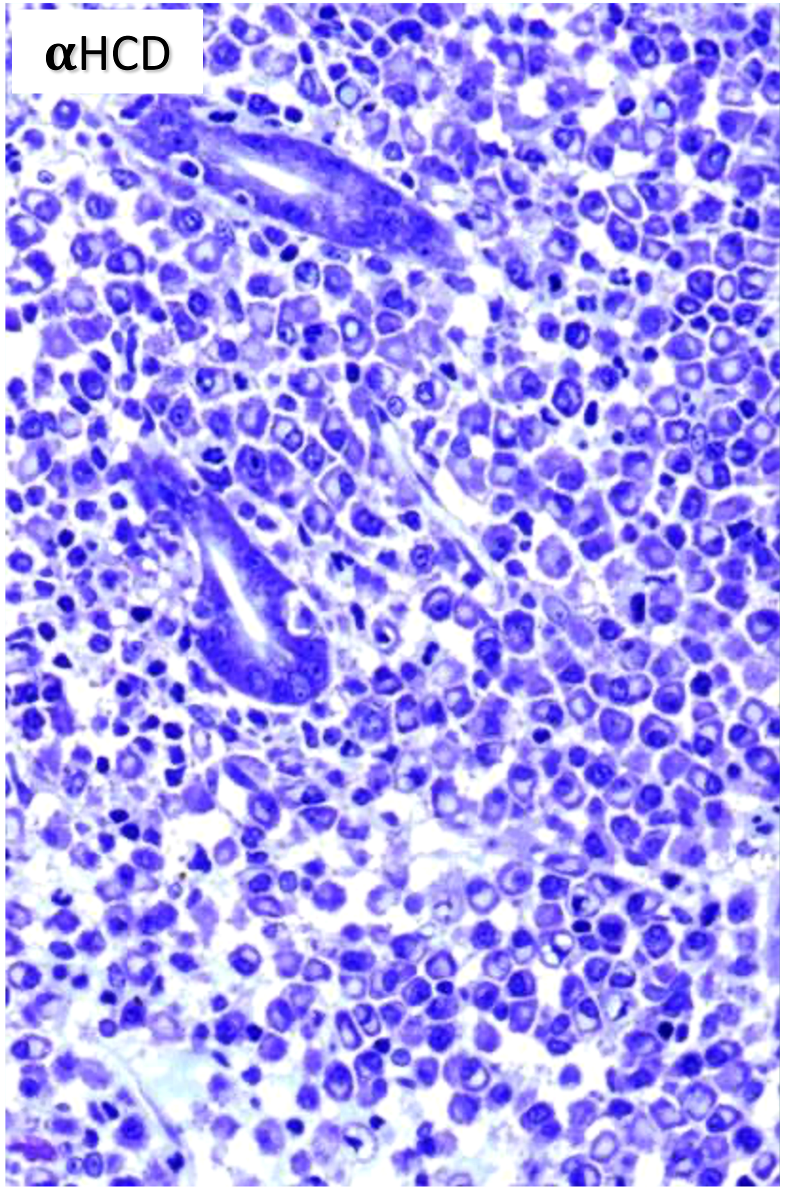
- riarrangiamenti di MALT1 (40%)
- Riarrangiamenti IGH (verosimili t1;14)
- Mutazioni di attivanti NF-kB mutualmente esclusive con traslocazioni *MALT1*
- In più dell’ 85% dei casi attivazione *NF-kB*

Linfoma marginale
del piccolo intestino
(Paz M 40aa con
perforazione)





CD20



ALPHA HEAVY CHIAN DISEASE

- (IPSID: Immuno-Proliferative Small Intestine Disease; linfoma medi-terraneo)
- LZM a marcatissima differenziazione plasmacellulare (DD plasmocitoma extramidollare)
- Raro; area mediterraneo, a basso livello socio-economico, con infezioni GI frequenti
- Pazienti II-III decade
- Intestino: duodeno > digiuno > ileo
- sindrome da malassorbimento, diarrea intermittente e dolore addominale della durata da alcuni mesi ad anni, episodi occlusione intestinale

Mutazioni puntiformi delezioni/inserzioni durante processo di ipermutazione somatica con conseguente difettiva sintesi della CH1 delle catene pesanti **α**

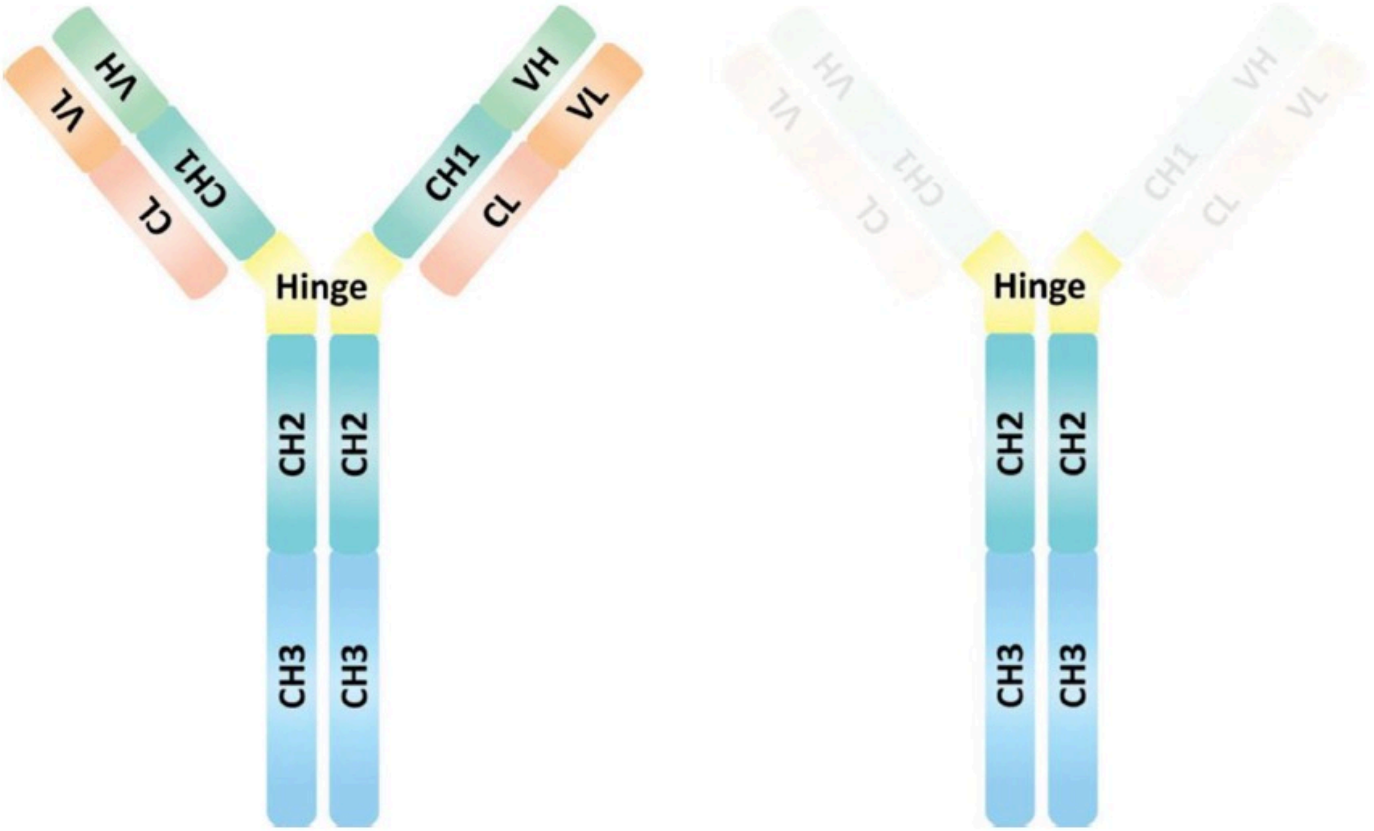
αHC in assenza di catena leggera in

Siero, urine e fluidi corporei

Elettroforesi sierica normale,

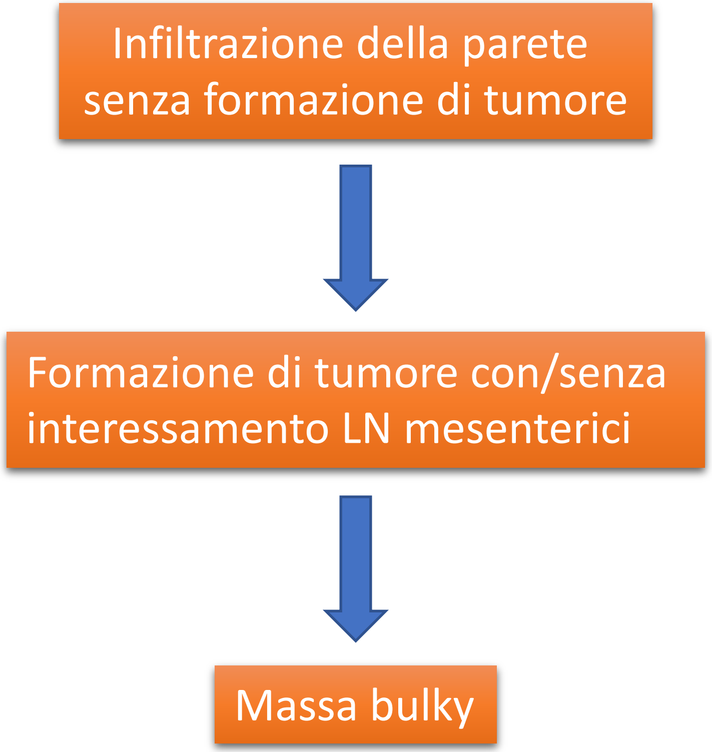
riscontro **α**HC patologica con immunofissazione e immunoelettoforesi

Bianchi Current Gastroenterology report 2018


VL
VH
CH1
CL
VH
VL
CH1
CL
Hinge
CH2
CH2
CH3
CH3
VL
VH
CH1
CL
VH
VL
CH1
CL
Hinge
CH2
CH2
CH3
CH3

Campylobacter jejuni:

- Gram-negativo a forma di elica
- rappresenta una delle cause più comuni di gastroenterite nel mondo
- ipotesi patogenetica: Infezioni ricorrenti inducono stato di immunoparesi che impedisce clearance CJ e lo stimolo Ag cronico porta accumulo pc IgA
- danno genomico può indurre αHCD
- assenza traslocazioni del EMZL
- Predisposizione individuale (specifici HLA o gruppi sanguigni)



Infiltrazione della parete senza formazione di tumore

In fase precoce sensibile ad antibiotici

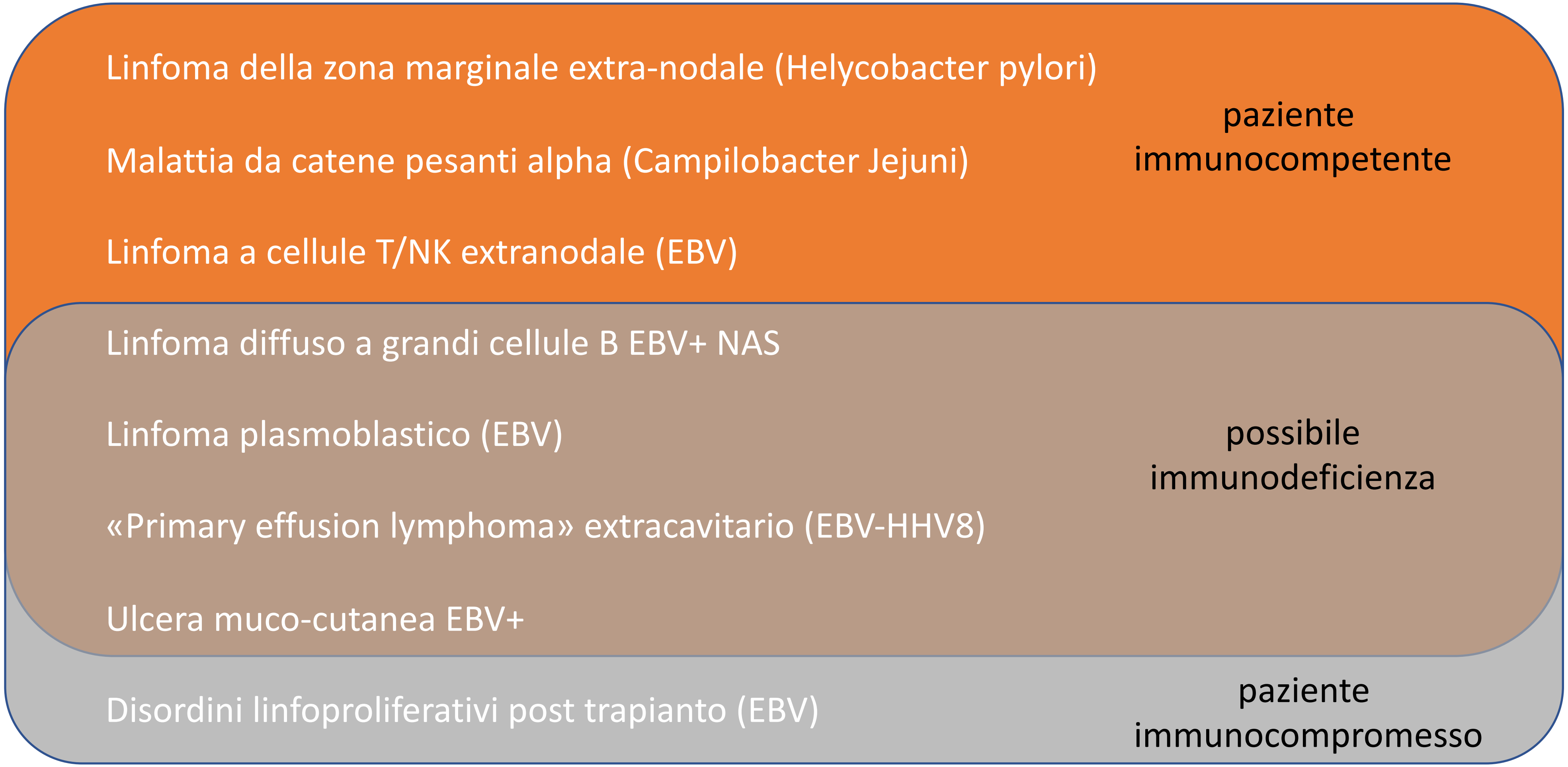
↓

Formazione di tumore con/senza interessamento LN mesenterici

↓

Massa bulky

Disordini linfoproliferativi correlati ad infezioni nel tratto gastroenterico



Linfoma della zona marginale extra-nodale (Helycobacter pylori)

Malattia da catene pesanti alpha (Campilobacter Jejuni)

Linfoma a cellule T/NK extranodale (EBV)

paziente
immunocompetente

Linfoma diffuso a grandi cellule B EBV+ NAS

Linfoma plasmoblastico (EBV)

«Primary effusion lymphoma» extracavitario (EBV-HHV8)

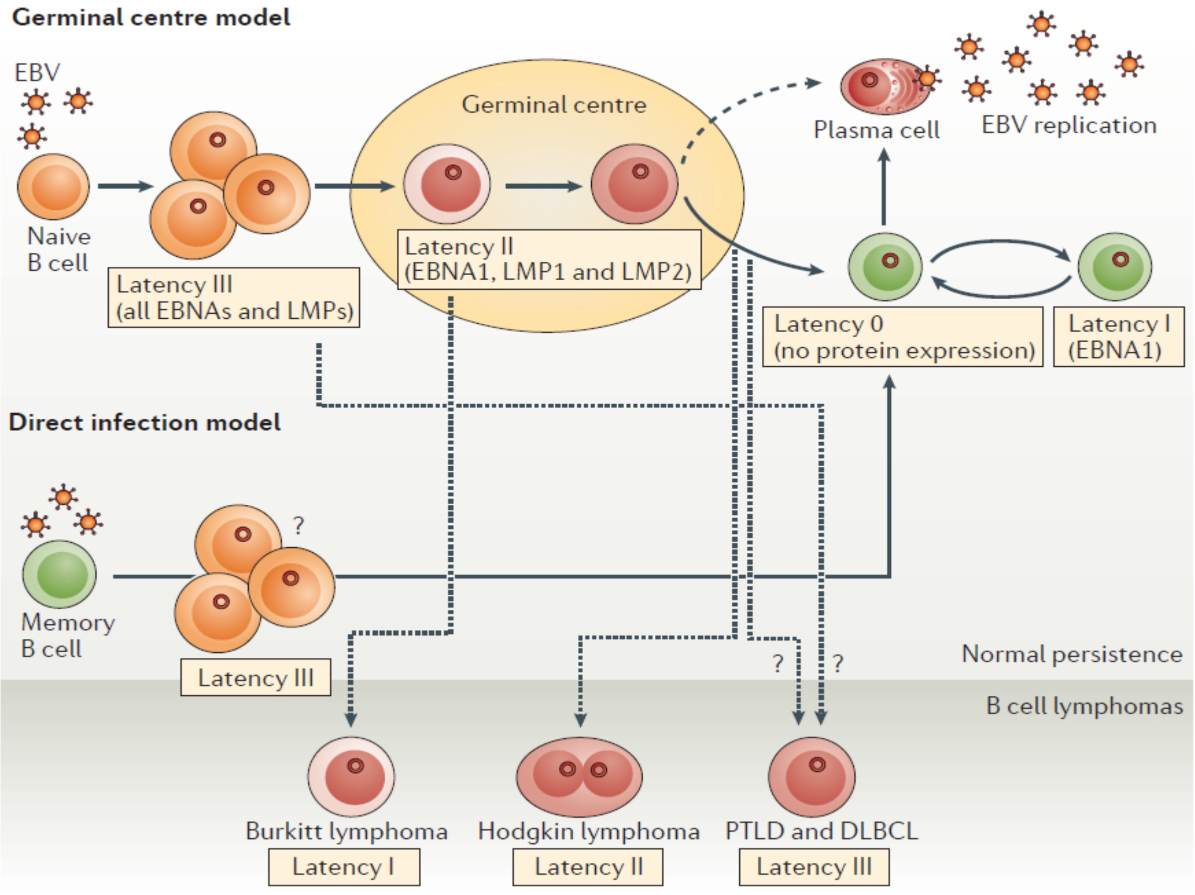
Ulcera muco-cutanea EBV+

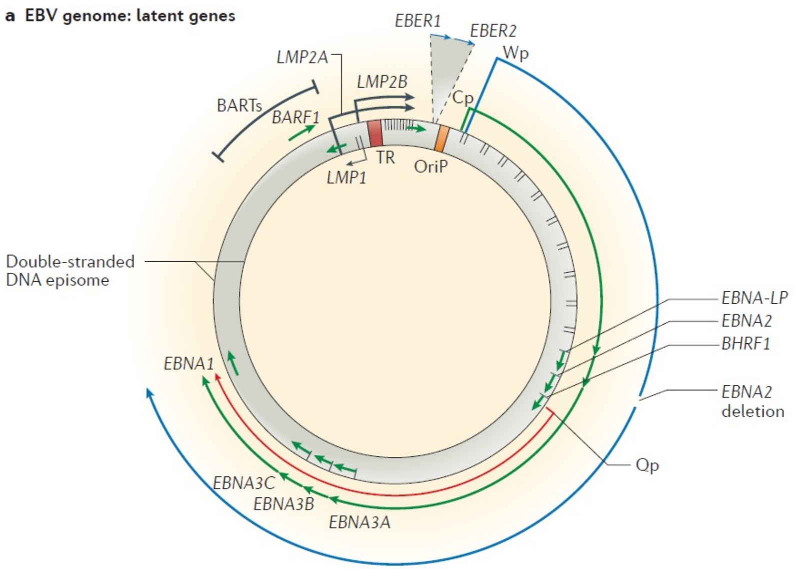
possibile
immunodeficienza

Disordini linfoproliferativi post trapianto (EBV)

paziente
immunocompromesso

EBV


Germinal centre model
EBV
Naive B cell
Latency III (all EBNAs and LMPs)
Germinal centre
Latency II (EBNA1, LMP1 and LMP2)
Plasma cell
EBV replication
Latency 0 (no protein expression)
Latency I (EBNA1)
Direct infection model
Memory B cell
?
Latency III
Normal persistence
B cell lymphomas
?
?
Burkitt lymphoma
Latency I
Hodgkin lymphoma
Latency II
PTLD and DLBCL
Latency III


a EBV genome: latent genes
EBER1
EBER2
Wp
LMP2A
LMP2B
BARTs
BARF1
Cp
TR
OriP
LMP1
Double-stranded DNA episome
EBNA-LP
EBNA2
BHRF1
EBNA2 deletion
EBNA1
Qp
EBNA3C
EBNA3B
EBNA3A

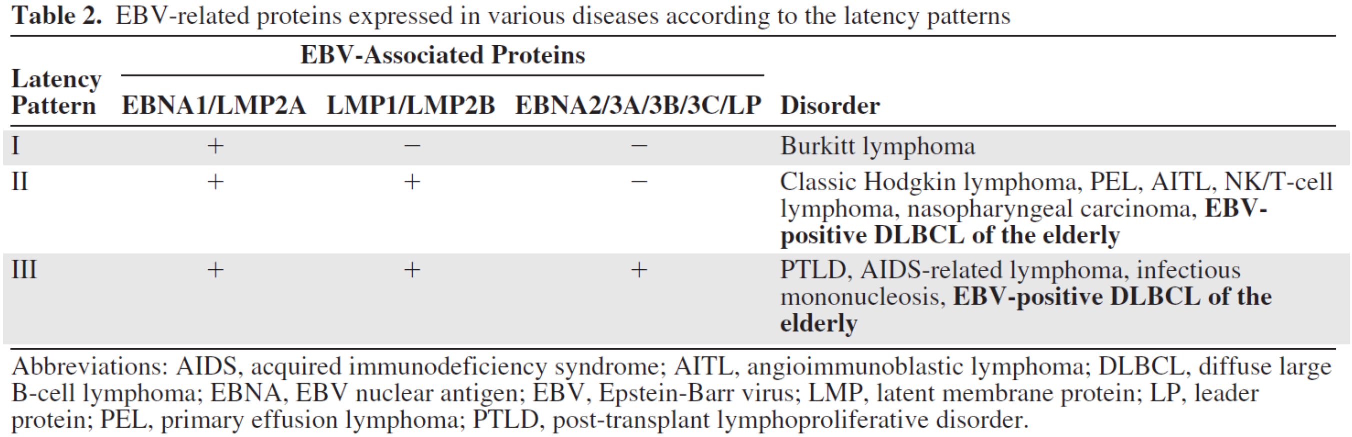
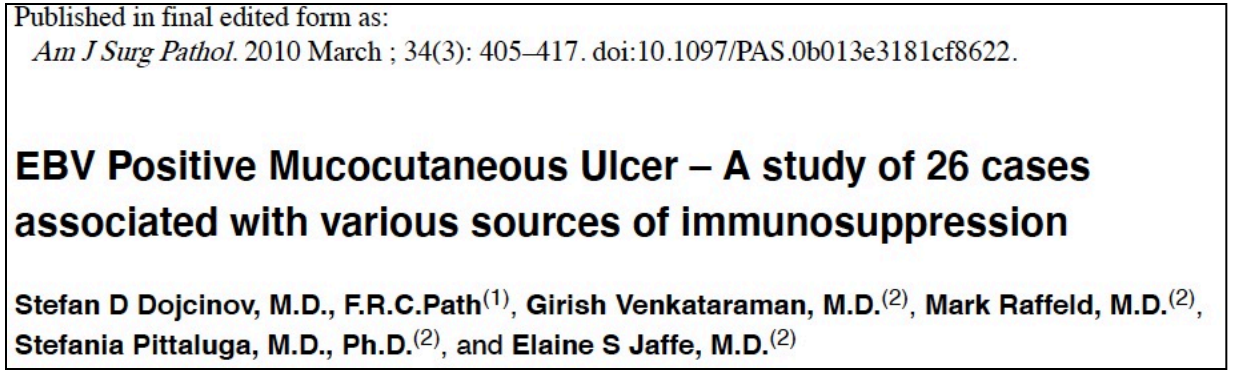


Table 2. EBV-related proteins expressed in various diseases according to the latency patterns

Latency Pattern	EBV-Associated Proteins			Disorder
	EBNA1/LMP2A	LMP1/LMP2B	EBNA2/3A/3B/3C/LP	
I	+	–	–	Burkitt lymphoma
II	+	+	–	Classic Hodgkin lymphoma, PEL, AITL, NK/T-cell lymphoma, nasopharyngeal carcinoma, **EBV-positive DLBCL of the elderly**
III	+	+	+	PTLD, AIDS-related lymphoma, infectious mononucleosis, **EBV-positive DLBCL of the elderly**

Abbreviations: AIDS, acquired immunodeficiency syndrome; AITL, angioimmunoblastic lymphoma; DLBCL, diffuse large B-cell lymphoma; EBNA, EBV nuclear antigen; EBV, Epstein-Barr virus; LMP, latent membrane protein; LP, leader protein; PEL, primary effusion lymphoma; PTLD, post-transplant lymphoproliferative disorder.

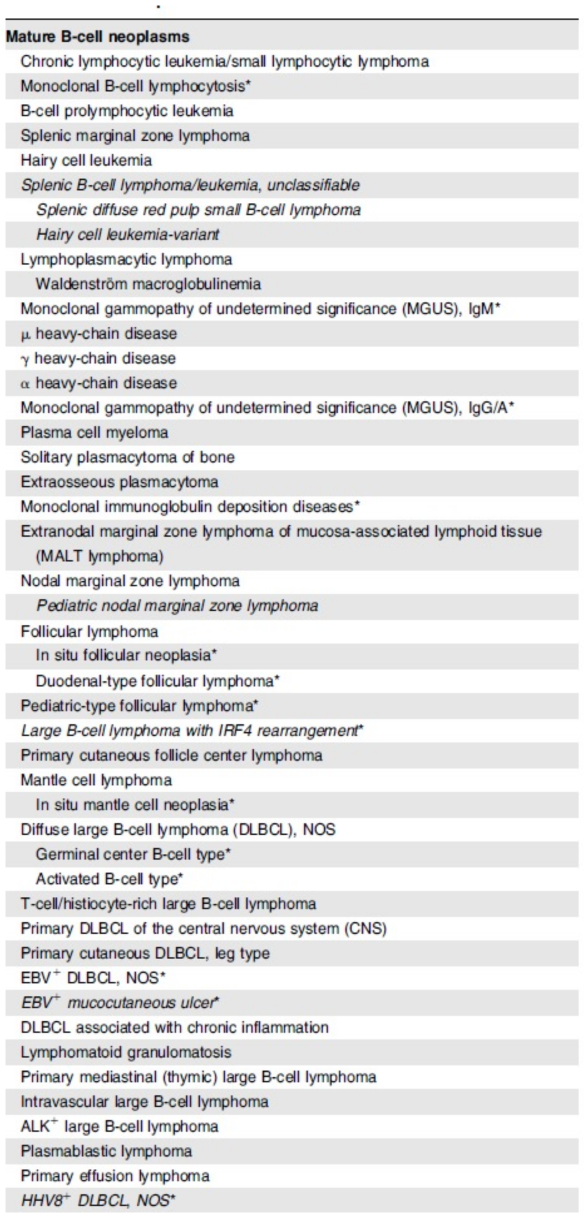
EBV positive
Mucocutaneous Ulcer (EBVMCU)


Published in final edited form as:
Am J Surg Pathol. 2010 March ; 34(3): 405–417. doi:10.1097/PAS.0b013e3181cf8622.

EBV Positive Mucocutaneous Ulcer – A study of 26 cases associated with various sources of immunosuppression

Stefan D Dojcinov, M.D., F.R.C.Path(1), **Girish Venkataraman, M.D.**(2), **Mark Raffeld, M.D.**(2), **Stefania Pittaluga, M.D., Ph.D.**(2), and **Elaine S Jaffe, M.D.**(2)

Entità provvisoria
nella classificazione WHO 2017;
non è considerato linfoma
ma disordine linfoproliferativo


Mature B-cell neoplasms

- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Monoclonal B-cell lymphocytosis*
- B-cell prolymphocytic leukemia
- Splenic marginal zone lymphoma
- Hairy cell leukemia
- *Splenic B-cell lymphoma/leukemia, unclassifiable*
  - *Splenic diffuse red pulp small B-cell lymphoma*
  - *Hairy cell leukemia-variant*
- Lymphoplasmacytic lymphoma
  - Waldenström macroglobulinemia
- Monoclonal gammopathy of undetermined significance (MGUS), IgM*
- μ heavy-chain disease
- γ heavy-chain disease
- α heavy-chain disease
- Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*
- Plasma cell myeloma
- Solitary plasmacytoma of bone
- Extraosseous plasmacytoma
- Monoclonal immunoglobulin deposition diseases*
- Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Nodal marginal zone lymphoma
  - *Pediatric nodal marginal zone lymphoma*
- Follicular lymphoma
  - In situ follicular neoplasia*
  - Duodenal-type follicular lymphoma*
- Pediatric-type follicular lymphoma*
- *Large B-cell lymphoma with IRF4 rearrangement**
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
  - In situ mantle cell neoplasia*
- Diffuse large B-cell lymphoma (DLBCL), NOS
  - Germinal center B-cell type*
  - Activated B-cell type*
- T-cell/histiocyte-rich large B-cell lymphoma
- Primary DLBCL of the central nervous system (CNS)
- Primary cutaneous DLBCL, leg type
- EBV^+ DLBCL, NOS*
- *EBV^+ mucocutaneous ulcer**
- DLBCL associated with chronic inflammation
- Lymphomatoid granulomatosis
- Primary mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- ALK^+ large B-cell lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma
- *$HHV8^+$ DLBCL, NOS**

EBVUMC

- Ulcere solitarie, a margini netti, a lenta crescita
- sede: orofaringea (50%), cute (30%), GI (20%)
- mai formazione di masse, linfodenopatie generalizzate, organomegalie o coinvolgimento osteomidollare
- correlate a immunosoppressione iatrogena:
  metotrexate, ciclosporina, azatioprina, prednisolone
  tacrolimus, inibitori TNFα (infliximab), micofenolato mofetile
- correlazione con immunosenescenza (pazienti anziani), HIV

Nel tratto GI in pazienti:

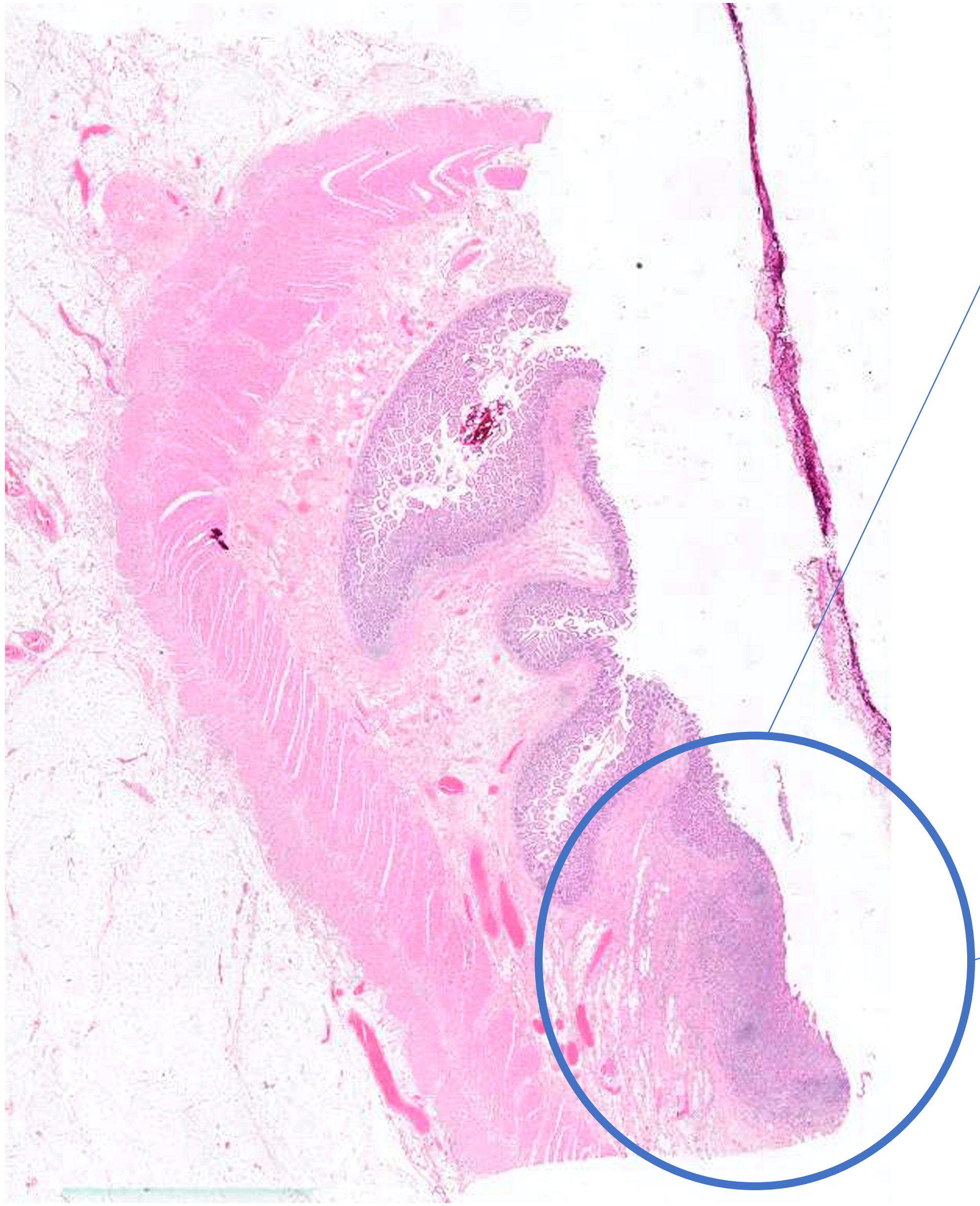
- immunosoppressi per trattamento di IBD (Crohn, RCU)
- artrite reumatoide
- post-trapianto
- trattati per linfoma
- coliti immunorelate (post trattamento ICPI anti CTLA4 /PD1)
- diverticolite

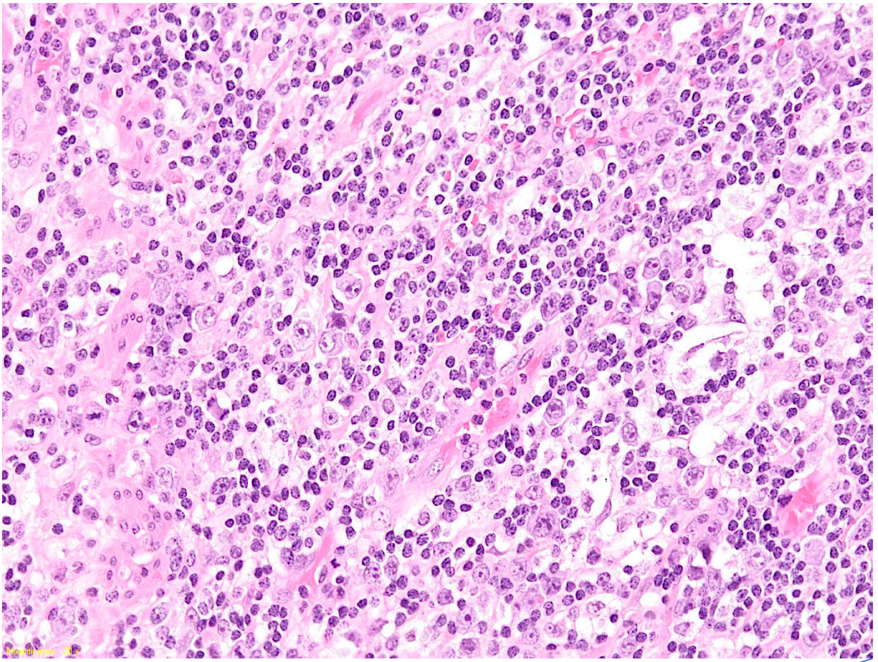
EBVMCU è caratterizzata da un decorso autolimitante con remissioni spontanee

o regressione dopo riduzione o sospensione della terapia immunosoppressiva

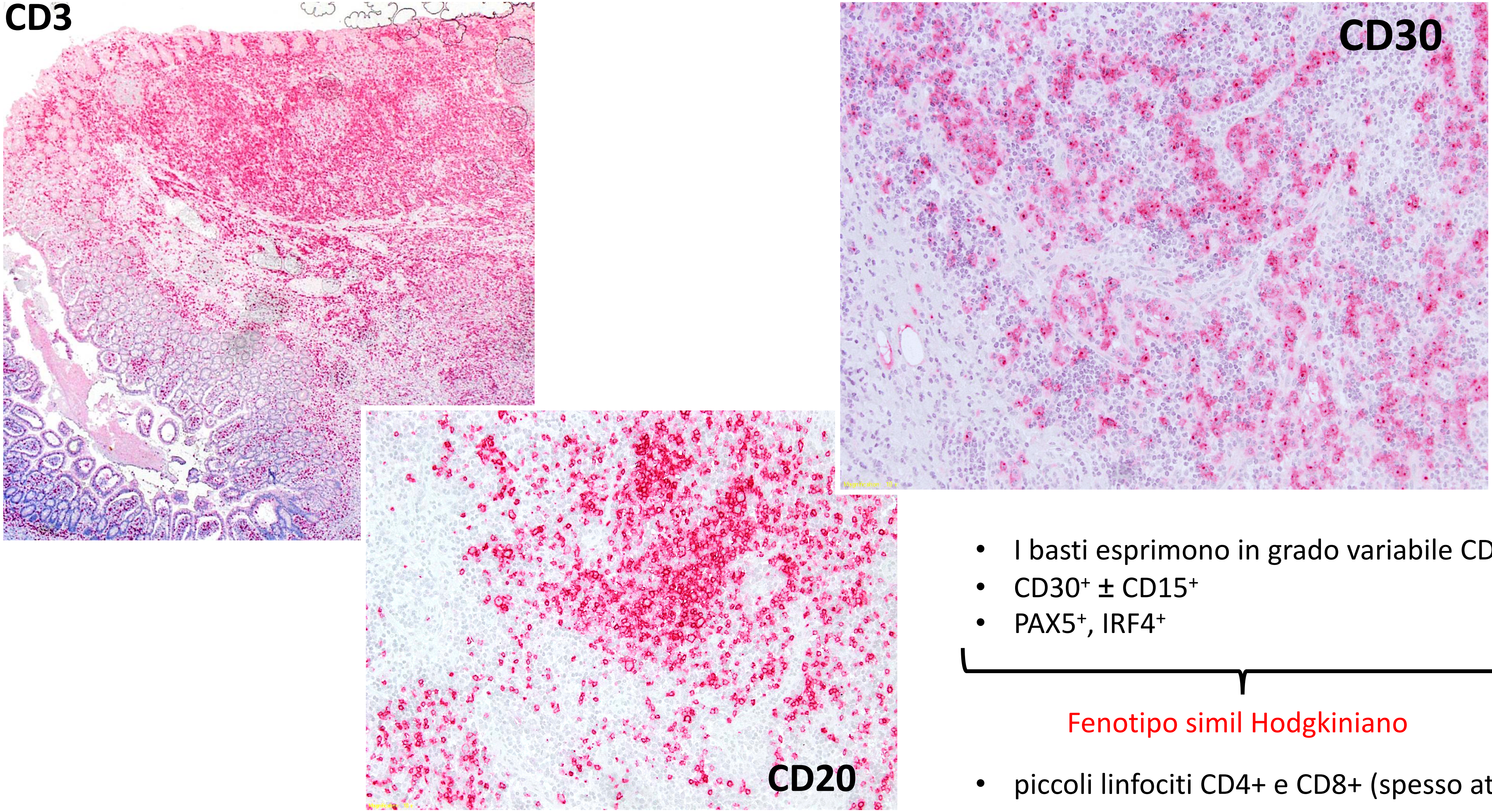
(Ishigava Cancers 2021, Zanelli Cancers 2021)

Ulcera ileale





- Grandi cellule sparse citologia immunoblastica o simil Reed-sternberg, o in apoptosi
- piccoli linfociti, eosinofili, istiociti, plasmacellule
- rima di piccoli linfociti alla base

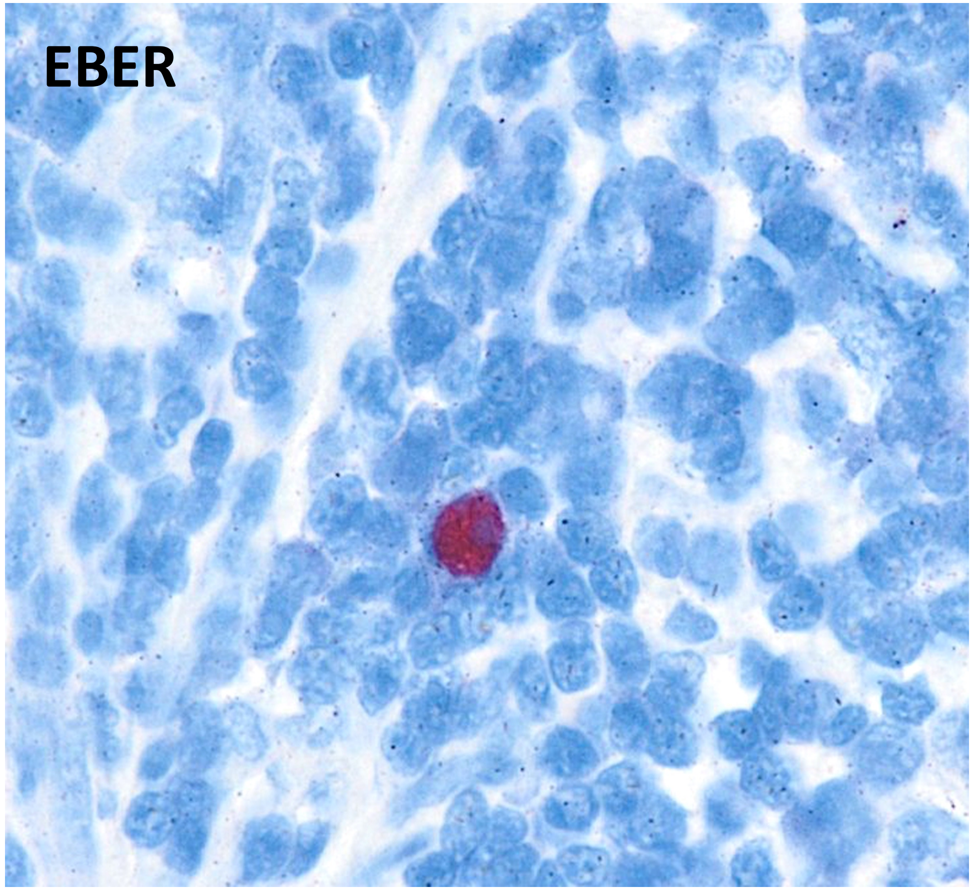


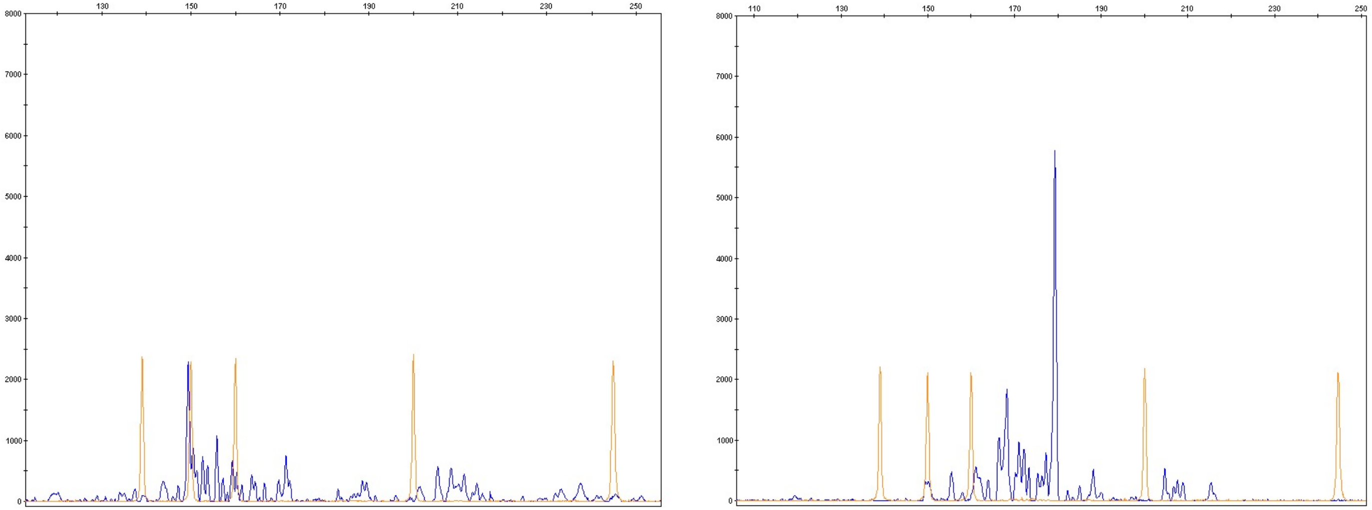
- I basti esprimono in grado variabile CD20
- CD30⁺ ± CD15⁺
- PAX5⁺, IRF4⁺

Fenotipo simil Hodgkiniano

- piccoli linfociti CD4+ e CD8+ (spesso attivati)

- EBV+ in piccole grandi cellule
- 30% *IG* monoclonali
- Possibile riscontro mono/oligo cloni T: riduzione della diversità del repertorio del TCR legata alla senescenza





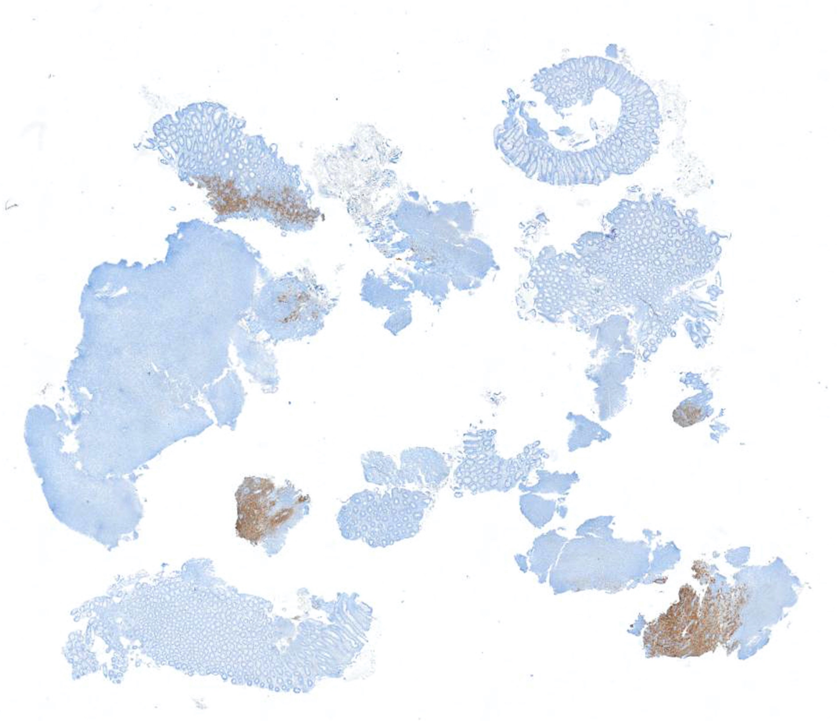
EBVMCU: prognosi e terapia

- Andamento indolente autolimitante
- in caso di immunosoppressione iatrogena

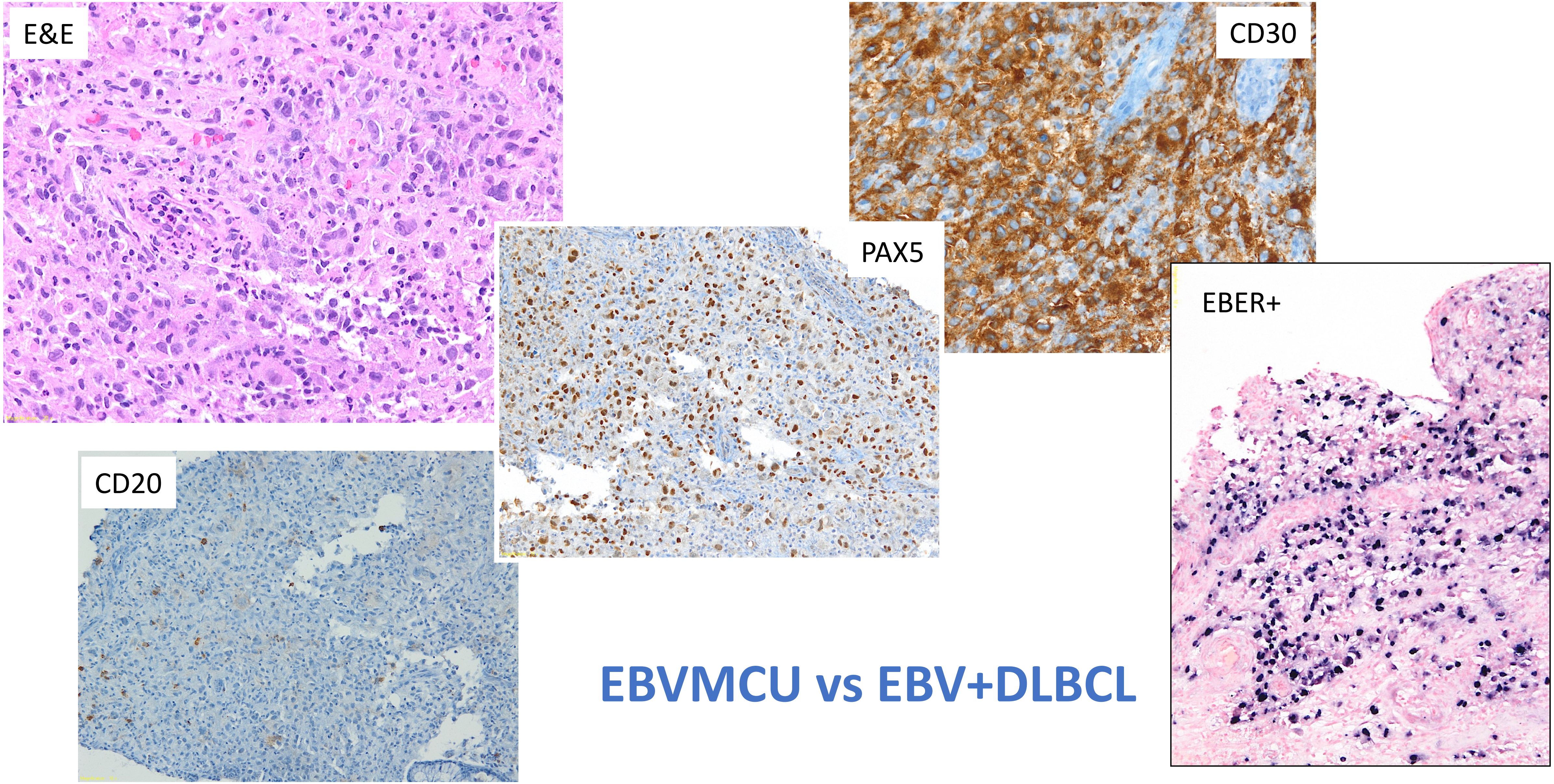
  una riduzione/interruzione del farmaco induce remissione
- possibile andamento con remissioni/recidive
- EBVMCU in post-linfoma e IBD possibili ulcere multiple
- in coliti immunorelate possibili perforazioni
- raramente evoluzione a linfoma (in IBD)
- possibile terapia: chirurgica, anti CD20/anti CD30,

  radioterapia (o combinazioni)

Attenzione alla diagnosi differenziale



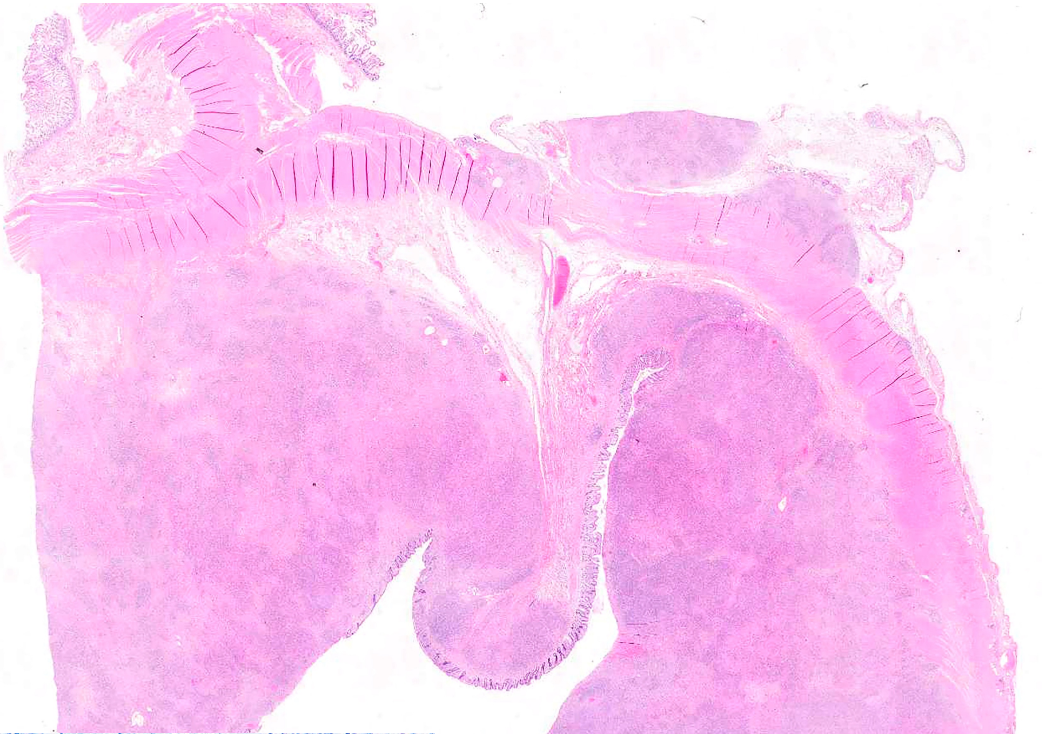
lesione del sigma CD30+

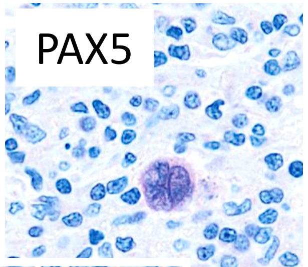

E&E
CD30
PAX5
EBER+
CD20

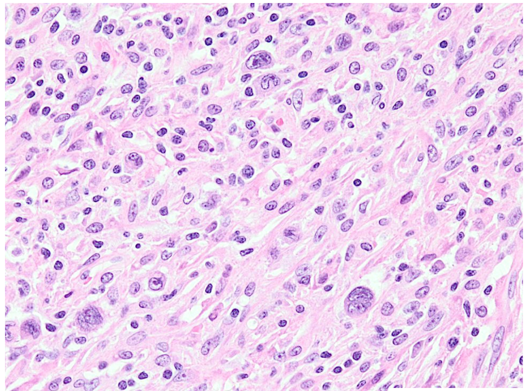
EBVMCU vs EBV+DLBCL

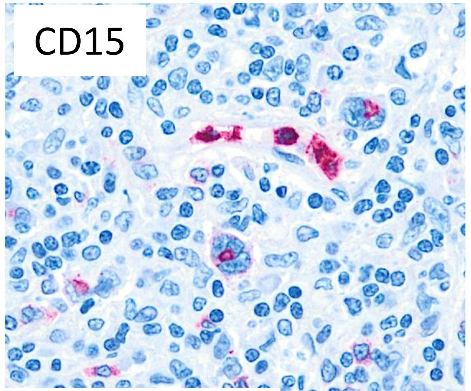
EBVMCU vs Hodgkin classico

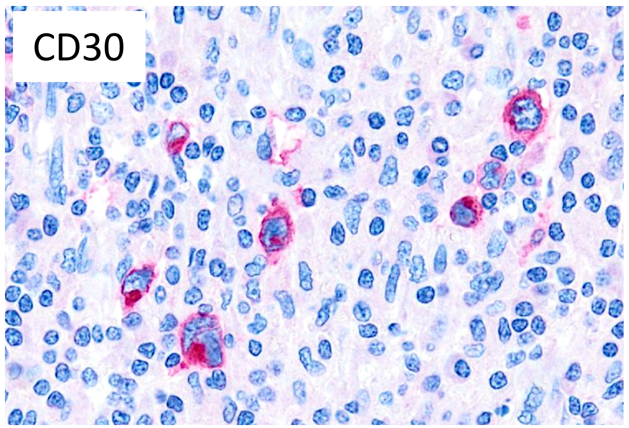
- Paziente di 39 aa in terapia per RCU
- EBVMCU non forma masse

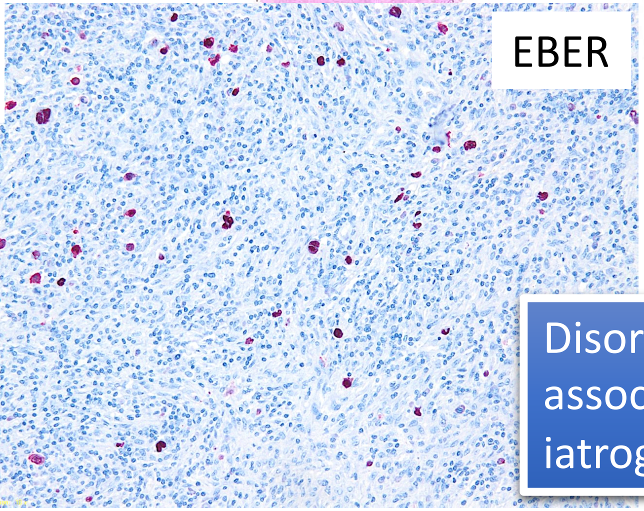












Disordine linfoproliferativo associato a immunospppressione iatrogena tipo cHL