Anaplastic large cell lymphoma

#*Stefano A. Pileri

#Unit of Haematopathology – European Institute of Oncology, Milan

*Bologna University School of Medicine, Bologna, Italy

2015... 2018
T-Cell Lymphomas: we are close to the finalization

Bologna
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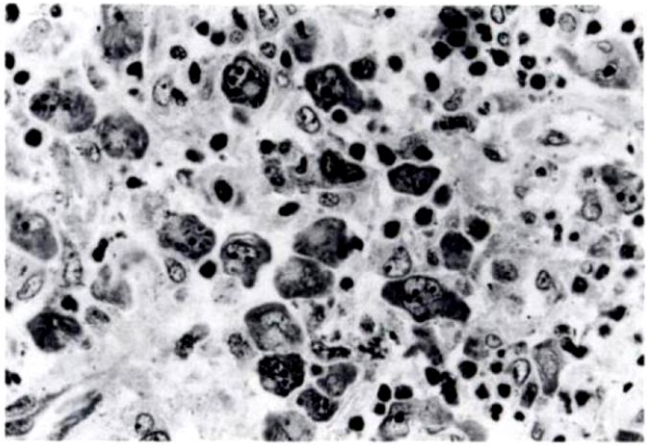
Takeda					+	+	

Anaplastic large cell lymphoma (ALCL) was first described by Stein et al. (Blood, 66:848-58) in 1985.

The tumour – previously often misdiagnosed as malignant histiocytosis or metastatic involvement by occult carcinoma – was characterised by distinctive morphology, cohesive growth pattern, frequent intra-sinusoidal diffusion, and regular expression of the lymphoid activation molecule Ki-1/CD30.



At that time, no distinction was made among anaplastic large cell lymphoid tumours carrying T, null or B-cell phenotype.

- **REAL Classification (Harris NL et al, Blood, 1994):**

  DLBCL, anaplastic variant;

  ALCL T/null (CT, LH, SC, GCR) (primary systemic, cutaneous) = accepted entity;

  ALCL Hodgkin's-like (ex-HR) = provisional entity.

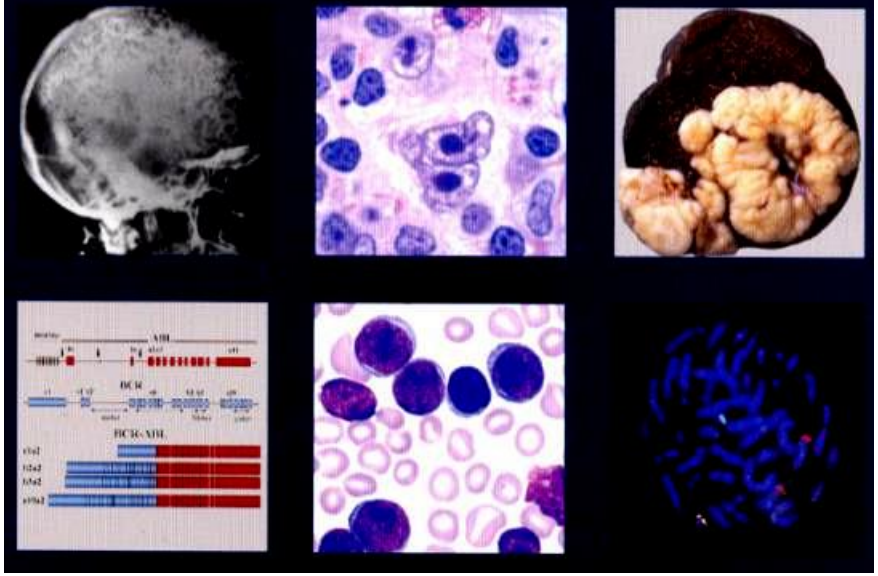
World Health Organization Classification of Tumours

2001

Pathology & Genetics

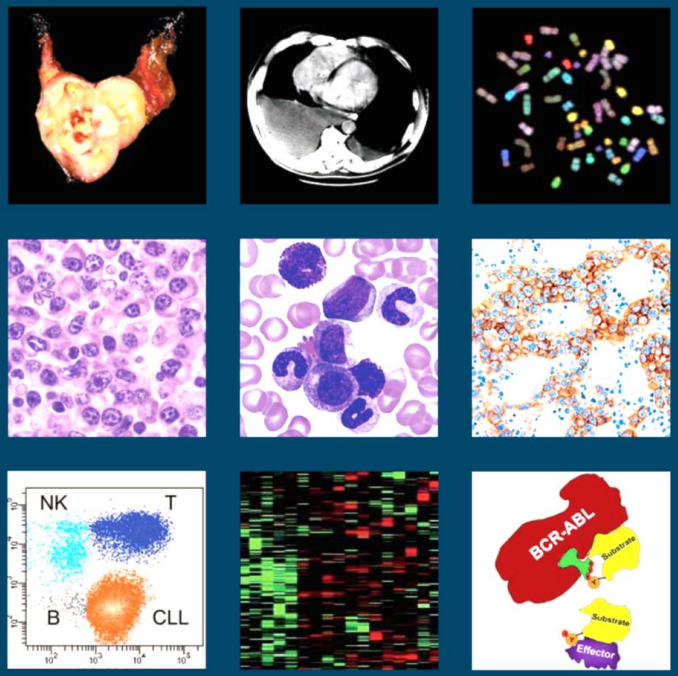
Tumours of Haematopoietic and Lymphoid Tissues

Edited by Elaine S. Jaffe, Nancy Lee Harris, Harald Stein, James W. Vardiman



WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

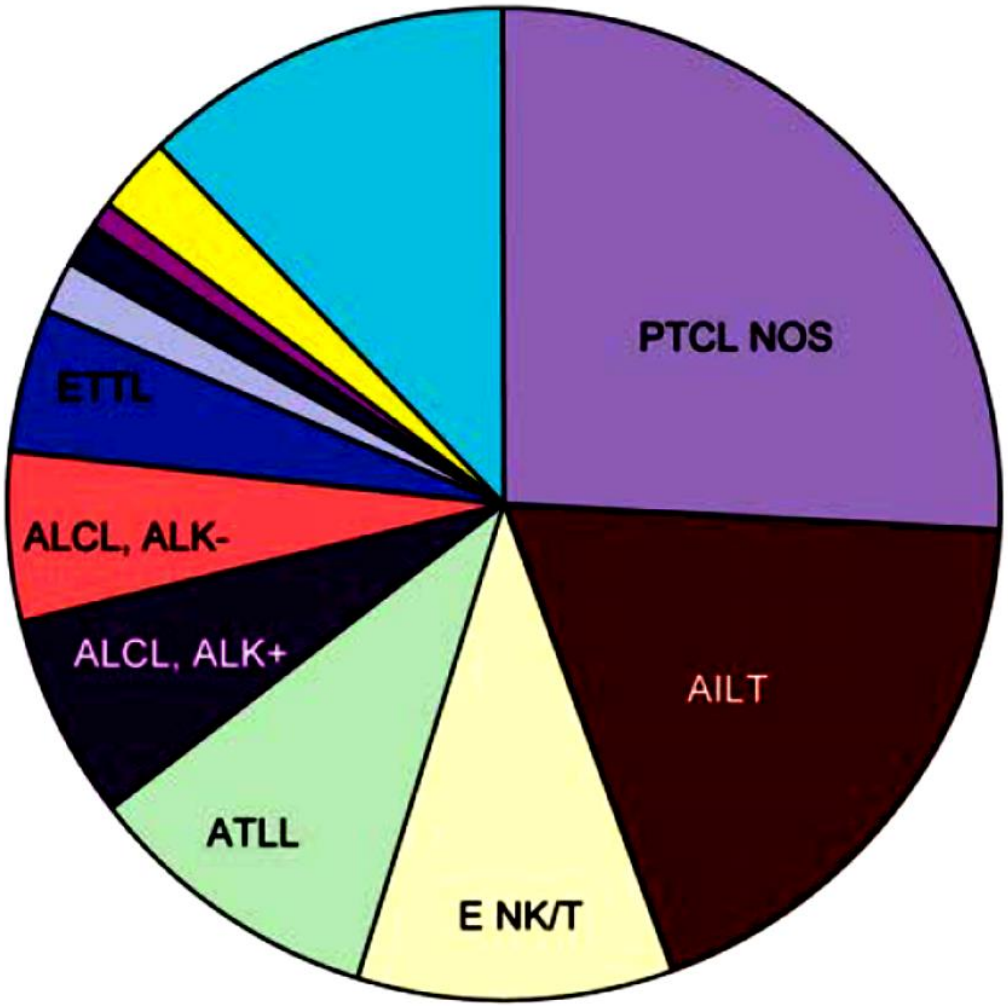
Edited by Steven H. Swerdlow, Elias Campo, Nancy Lee Harris, Elaine S. Jaffe, Stefano A. Pileri, Harald Stein, Jürgen Thiele, James W. Vardiman



WHO

2008

Peripheral T-cell Lymphomas



- Peripheral T-cell Lymphoma - NOS 25.9%
- Angioimmunoblastic 18.5%
- Natural killer/T-cell lymphoma 10.4%
- Adult T-cell leukemia/lymphoma 9.6%
- Anaplastic large cell lymphoma, ALK+ 6.6%
- Anaplastic large cell lymphoma, ALK- 5.5%
- Enteropathy-type T-cell* 4.7%
- Primary cutaneous ALCL 1.7%
- Hepatosplenic T-cell 1.4%
- Subcutaneous panniculitis-like 0.9%
- Unclassifiable PTCL 2.5%
- Other disorders 12.2%

T-Cell Lymphomas in South America and Europe

Monica Bellei[1]
Carlos Sergio Chiattone[2]
Stefano Luminari[1]
Emanuela Anna Pesce[1]
Maria Elena Cabrera[3]
Carmino Antonio de Souza[4]
Raul Gabús[5]
Lucia Zoppegno[6]
Jorge Milone[7]
Astrid Pavlovsky[8]
Joseph Michael Connors[9]
Francine Mary Foss[10]
Steven Michael Horwitz[11]
Raymond Liang[12]
Silvia Montoto[13]
Stefano Aldo Pileri[14]
Aaron Polliack[15]
Julie Marie Vose[16]
Pier Luigi Zinzani[14]
Emanuele Zucca[17]
Massimo Federico[1]

	Overall	Europe	USA	South America	Middle/ Far East
PTCL-NOS	38	40	42	42	26
AITL	17	20	21	8	15
ALCL, ALK$^-$	13	14	9	23	6
ALCL, ALK$^+$	7	6	8	8	4
NK/T nasal, nasal type, lymphoma/leukemia	13	6	9	13	31
Other histologies	12	14	11	6	18

	Overall		Italy		United Kingdom		Others *	
	n	%	n	%	n	%	n	%
PTCL-NOS	127	40	99	41	19	41	9	33
AITL	63	20	47	19	10	22	6	22
ALCL, ALK$^-$	44	14	34	14	9	20	1	4
ALCL, ALK$^+$	21	6	18	8	2	4	1	4
NK/T nasal, nasal type	19	6	13	5	3	7	3	11
Enteropathy-type	22	7	17	7	2	4	3	11
Hepatosplenic	5	2	5	2	-	-	-	-
Other histologies	16	5	11	4	1	2	4	15
Subcutaneous panniculitis-like	4		3		1		-	
Peripheral γδ T-cell lymphomas	3		1		-		2	
Unclassifiable T/NK PTCLs	9		7		-		2	
Total	317		244		46		27	

Anaplastic large cell lymphoma, ALK positive

Anaplastic large cell lymphoma, ALK negative
(UPGRADED TO DEFINITE ENTITY)

Breast implant-associated ALCL

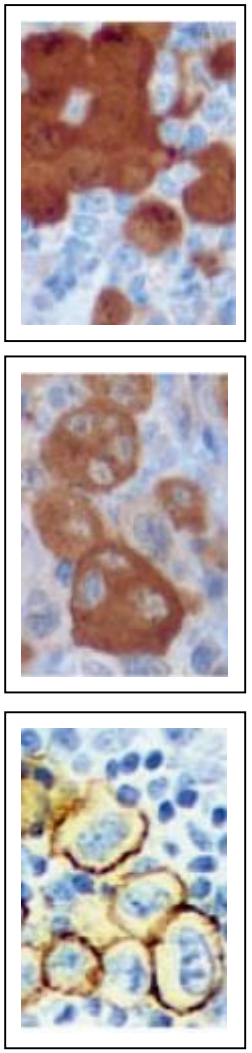
(NEW PROVISIONAL ENTITY)

Translocations and fusion proteins involving the ALK gene in ALK$^+$ ALCL

Table 1 Chromosomal translocations involving the ALK gene in human lymphoma

Disease	Chromosomal abnormalities	Fusion protein (kDa)	Partner gene	Frequency (%)	ALK IHC stains	Principal references
ALCL-DLBCL	t(2;5)(p23;q35)	NPM-ALK (80)	*NPM1*	75-80	Cyto/nuclear Nuclear	7, 18
ALCL-IMT	t(1;2)(q25;p23)	TPM3-ALK (104) (104)	*TPM3*	12-18	Cyto	45
ALCL	t(2;3)(p23;q21)	TGF-ALK 113,97.85)	*TFG*	2	Cyto	46, 47
ALCL-IMT	inv(2)(p23;q35)	ATIC-ALK (96)	*ATIC*	2	Cyto	48, 73
ALCL-IMT-DLBCL	t(2;17)(p23;q23)	CLTC1-ALK (250)	*CLTL1*	2	Cyto	49
ALCL	t(2;17)(p23;q25)	ALO17-ALK (ND)	*ALO17*	<1	Cyto	51
ALCL	t(2;X)(p32;q11-12)	MSN-ALK (125)	*MSN*	<1	Cyto	50, 73
ALCL-IMT	t(2;19)(p23;p13)	TPM4-ALK(95-105)	*TPM4*	<1	Cyto	73
ALCL	t(2;22)(p23;q11.2)	MYH9-ALK (220)	*MYH9*	<1	Cyto	52

Abbreviations: ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; ATIC, 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase; CLTL1, Clathrin heavy chainlike1; cyto, cytoplasmic; DLBCL, diffuse large B-cell lymphoma; MSN, moesin; NPM, nucleophosmin.

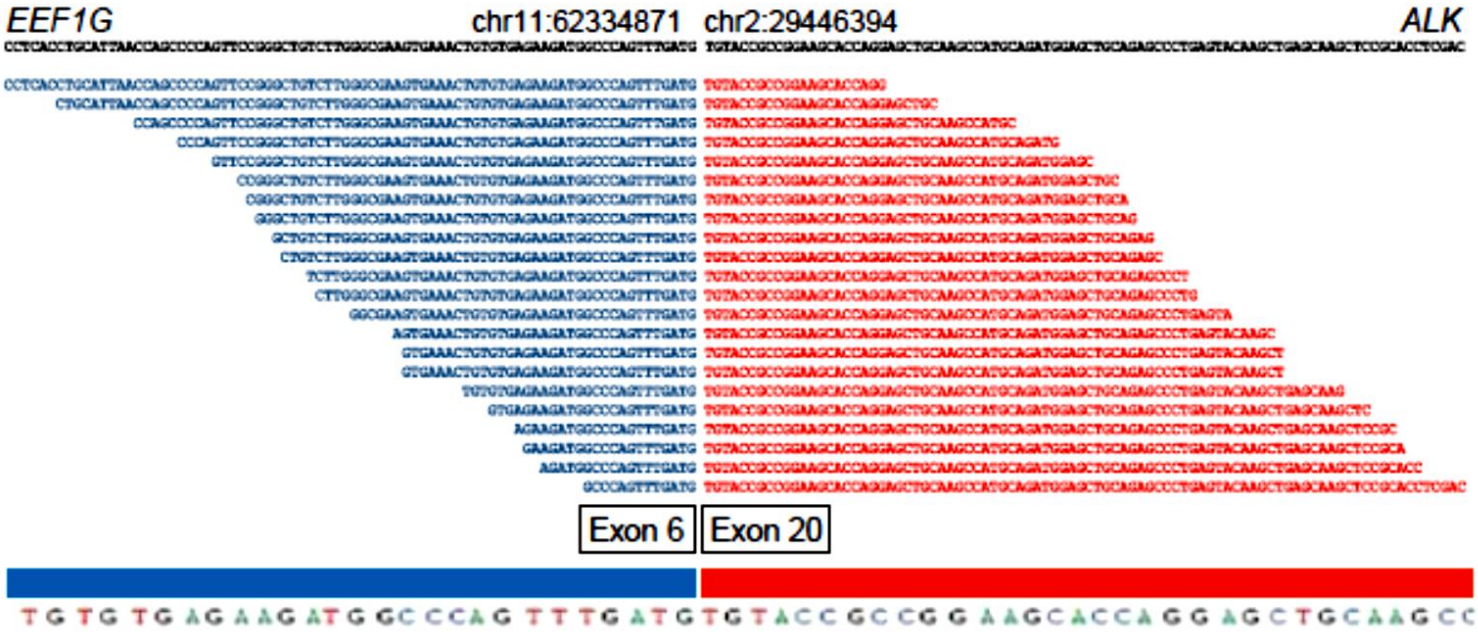


Anaplastic large-cell lymphoma.
Inghirami G and Pileri SA. Sem Diagn Pathol 2011; 28:190-201.

Novel ALK fusion in anaplastic large cell lymphoma involving EEF1G, a subunit of the eukaryotic elongation factor-1 complex

Leukemia (2017) **31,** 743–747; doi:10.1038/leu.2016.331

G Palacios[1], TI Shaw[2], Y Li[2], RK Singh[3], M Valentine[4], JT Sandlund[5], MS Lim[6], CG Mullighan[1] and V Leventaki[1]



Translocations and fusion proteins involving the ALK gene in ALK$^+$ ALCL

The oncogenic role of ALK fusion proteins

- Translocations involving ALK produce fusion proteins with constitutive tyrosine kinase activity in most cases deriving from spontaneous dimerization induced by the different fusion partners
- Transforming ability *in vitro*
- Tumorigenic role in transgenic mouse models
- Engagement of intracellular pathways

ALK, anaplastic lymphoma kinase.
Chiarle R, *et al.* Nat Rev Cancer 2008;8:11–23.

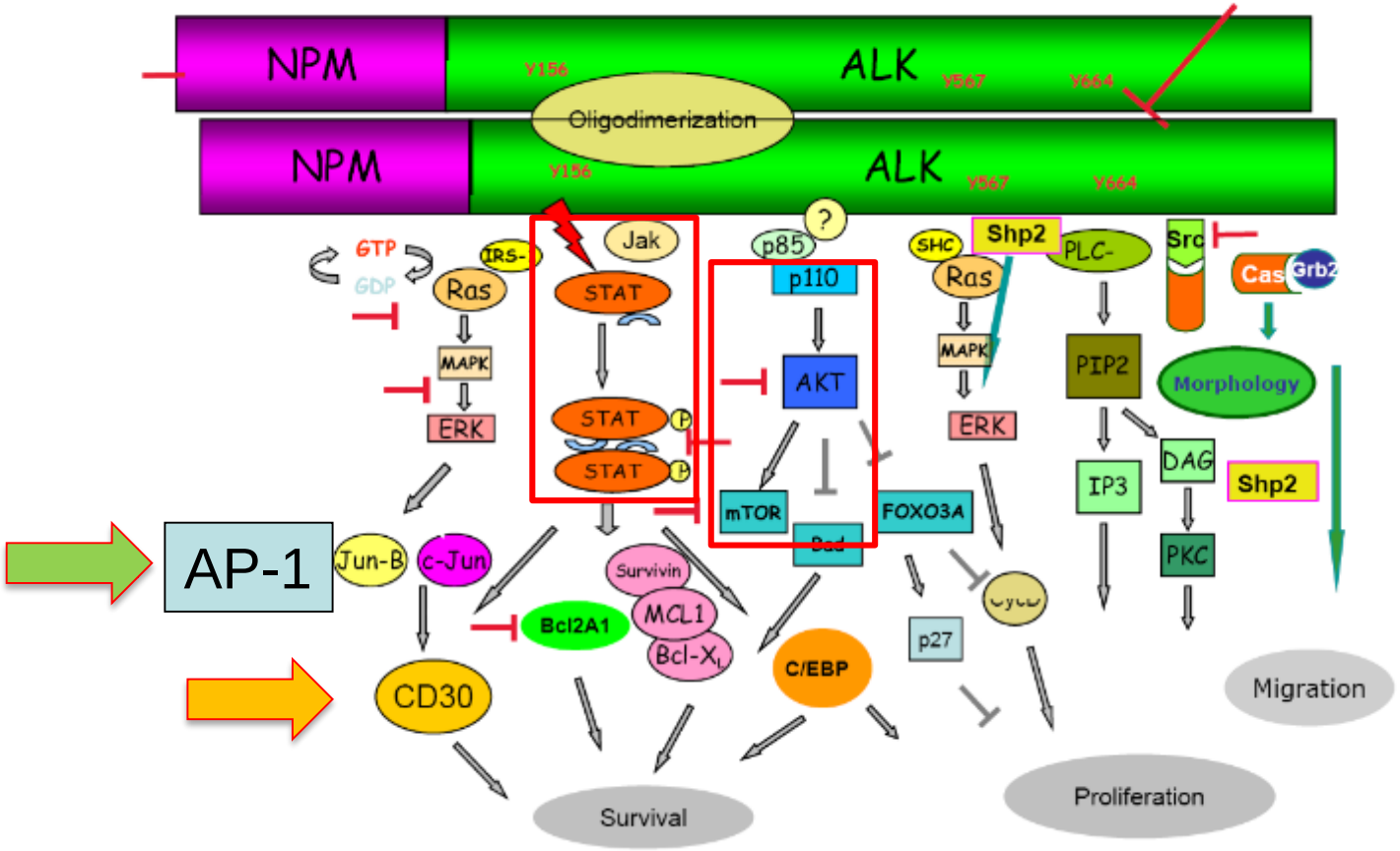
ALK+ ALCL

Anaplastic large-cell lymphoma

Seminars in Diagnostic Pathology (2011) 28, 190-201

Giorgio Inghirami, MD,[a,b] Stefano A. Pileri, MD,[c] and the European T-Cell Lymphoma Study Group

Small Molecule ALK-Tyrosine Kinase Inhibitors



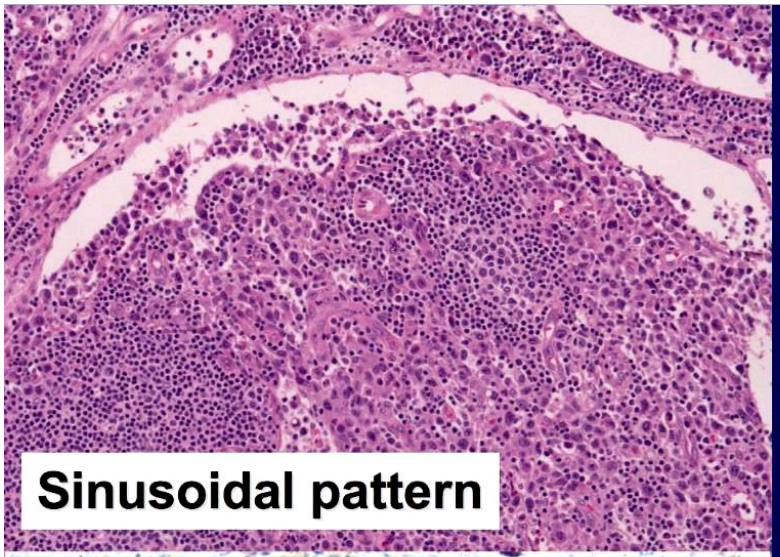
nature medicine

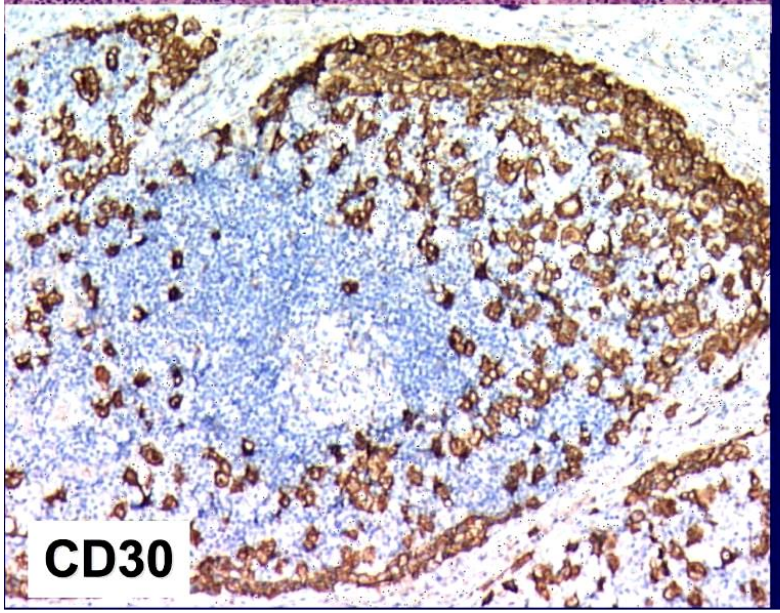
PDGFR blockade is a rational and effective therapy for NPM-ALK–driven lymphomas

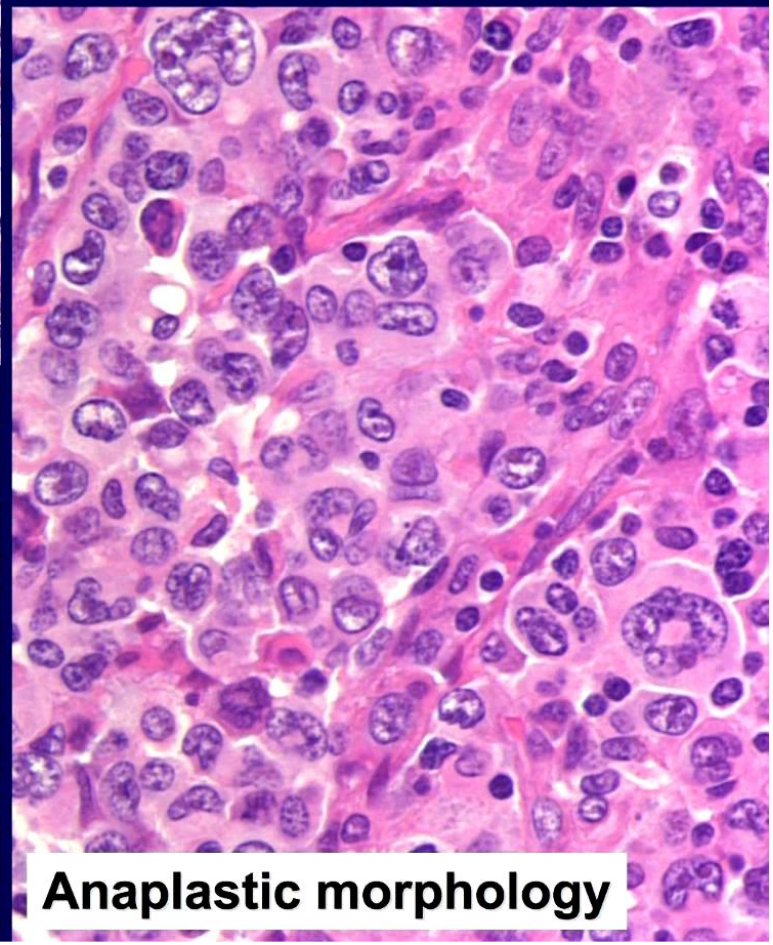
Daniela Laimer[1,25], Helmut Dolznig[2,25], Karoline Kollmann[3,25], Paul W Vesely[4,24,25], Michaela Schlederer[5], Olaf Merkel[6,24], Ana-Iris Schiefer[1], Melanie R Hassler[1,7], Susi Heider[1], Lena Amenitsch[1], Christiane Thallinger[7], Philipp B Staber[8,9], Ingrid Simonitsch-Klupp[1], Matthias Artaker[10], Sabine Lagger[10,24], Suzanne D Turner[11], Stefano Pileri[12], Pier Paolo Piccaluga[12], Peter Valent[13,14], Katia Messana[15], Indira Landra[15], Thomas Weichhart[2], Sylvia Knapp[16,17], Medhat Shehata[13], Maria Todaro[15], Veronika Sexl[3], Gerald Höfler[4], Roberto Piva[15,18], Enzo Medico[19,20], Bruce A Ruggeri[21], Mangeng Cheng[21], Robert Eferl[22], Gerda Egger[1], Josef M Penninger[23], Ulrich Jaeger[13], Richard Moriggl[5], Giorgio Inghirami[15,19] & Lukas Kenner[1,5]

Received 23 July; accepted 10 September; published online 14 October 2012; doi:10.1038/nm.2966

Anaplastic large cell lymphoma







Programmed Death Ligand 1 Is Expressed by Non–Hodgkin Lymphomas and Inhibits the Activity of Tumor-Associated T Cells

David J. Andorsky[1], Reiko E. Yamada[1], Jonathan Said[2], Geraldine S. Pinkus[3], David J. Betting[1], and John M. Timmerman[1]

Abstract

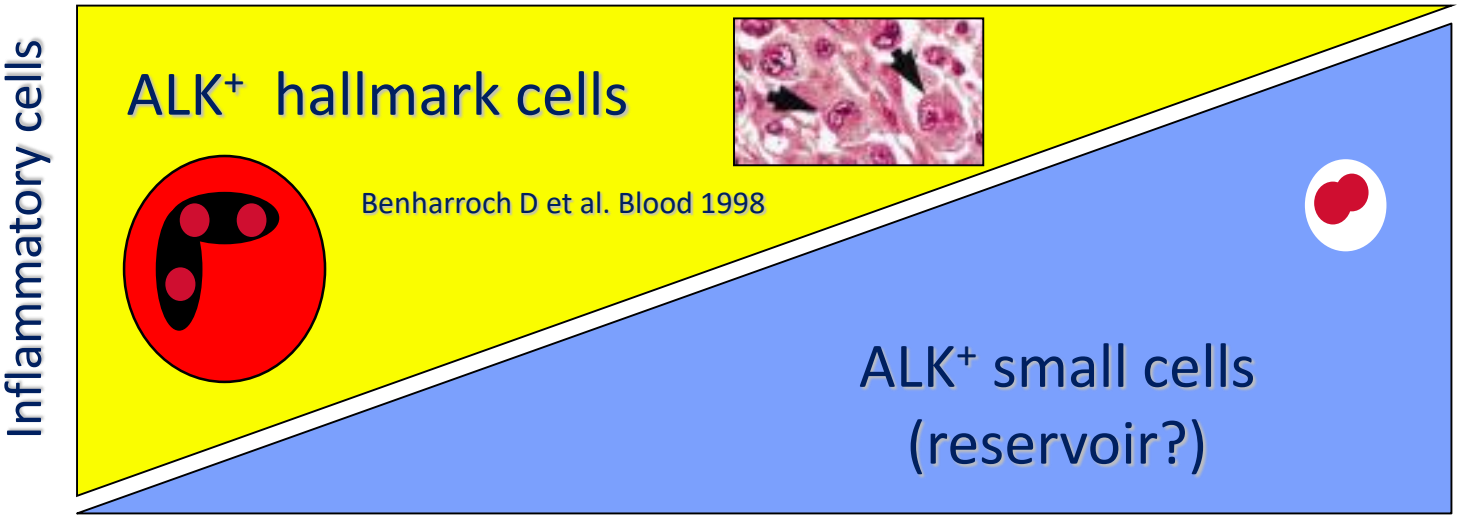
Purpose: Programmed death ligand 1 (PD-L1) is expressed on antigen-presenting cells and inhibits activation of T cells through its receptor PD-1. PD-L1 is aberrantly expressed on some epithelial malignancies and Hodgkin lymphomas and may prevent effective host antitumor immunity. The role of PD-L1 in non–Hodgkin lymphomas (NHL) is not well characterized.

Experimental Design: PD-L1 expression was analyzed in cell lines and lymphoma specimens by using flow cytometry and immunohistochemistry. Functional activity of PD-L1 was studied by incubating irradiated lymphoma cells with allogeneic T cells with or without anti-PD-L1 blocking antibody; T-cell proliferation and IFN-γ secretion served as measures of T-cell activation. Similar experiments were conducted using cultures of primary lymphoma specimens containing host T cells.

Results: PD-L1 was expressed uniformly by anaplastic large cell lymphoma (ALCL) cell lines, but rarely in B-cell NHL, confined to a subset of diffuse large B-cell lymphomas (DLBCL) with activated B-cell features (3 of 28 cell lines and 24% of primary DLBCL). Anti-PD-L1 blocking antibody boosted proliferation and IFN-γ secretion by allogeneic T cells responding to ALCL and DLBCL cells. In autologous cultures of primary ALCL and DLBCL, PD-L1 blockade enhanced secretion of inflammatory cytokines IFN-γ, granulocyte macrophage colony-stimulating factor, interleukin (IL)-1, IL-6, IL-8, IL-13, TNF-α, and macrophage inflammatory protein-1α. In establishing cell lines from an aggressive PD-L1$^+$ mature B-cell lymphoma, we also noted that PD-L1 expression could be lost under certain *in vitro* culture conditions.

Conclusions: PD-L1 may thwart effective antitumor immune responses and represents an attractive target for lymphoma immunotherapy. *Clin Cancer Res; 17(13); 4232–44. ©2011 AACR.*

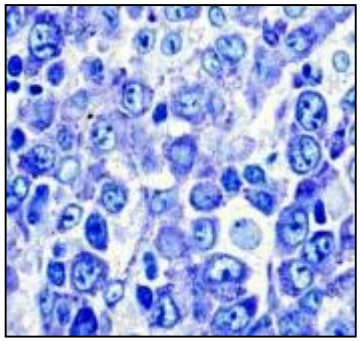
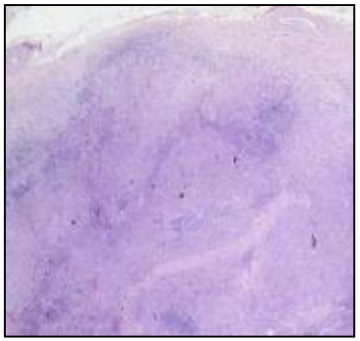
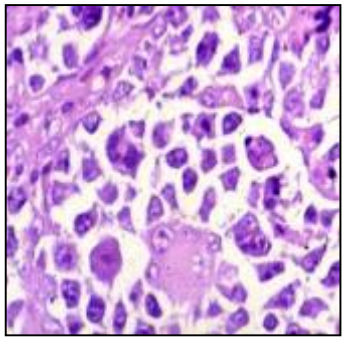
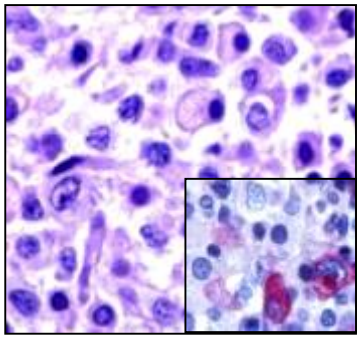
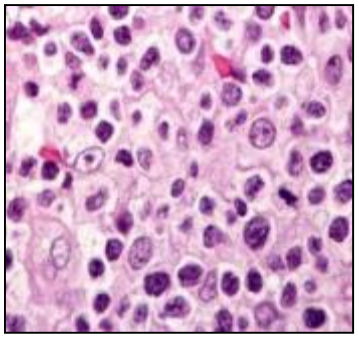
Morphologic spectrum of "ALK+ ALCL

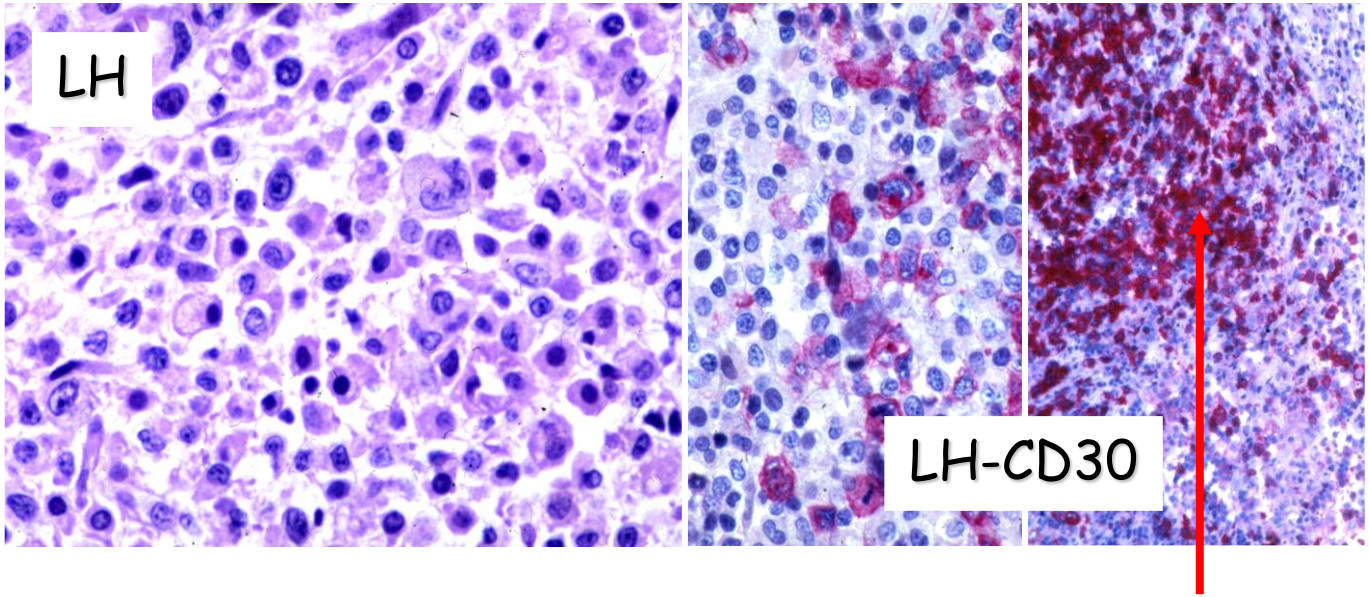


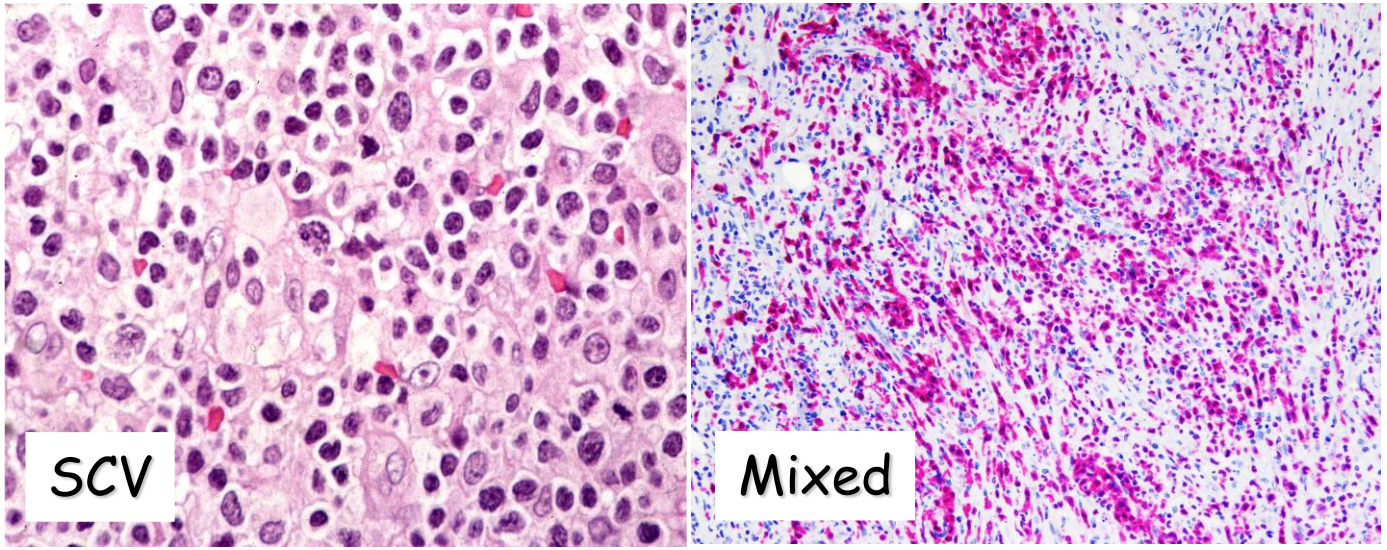
ALCL - CT
- HL

- mixed
(perivascular)

- SCV
- LH


LH
LH-CD30
Sheet of tumoural cells

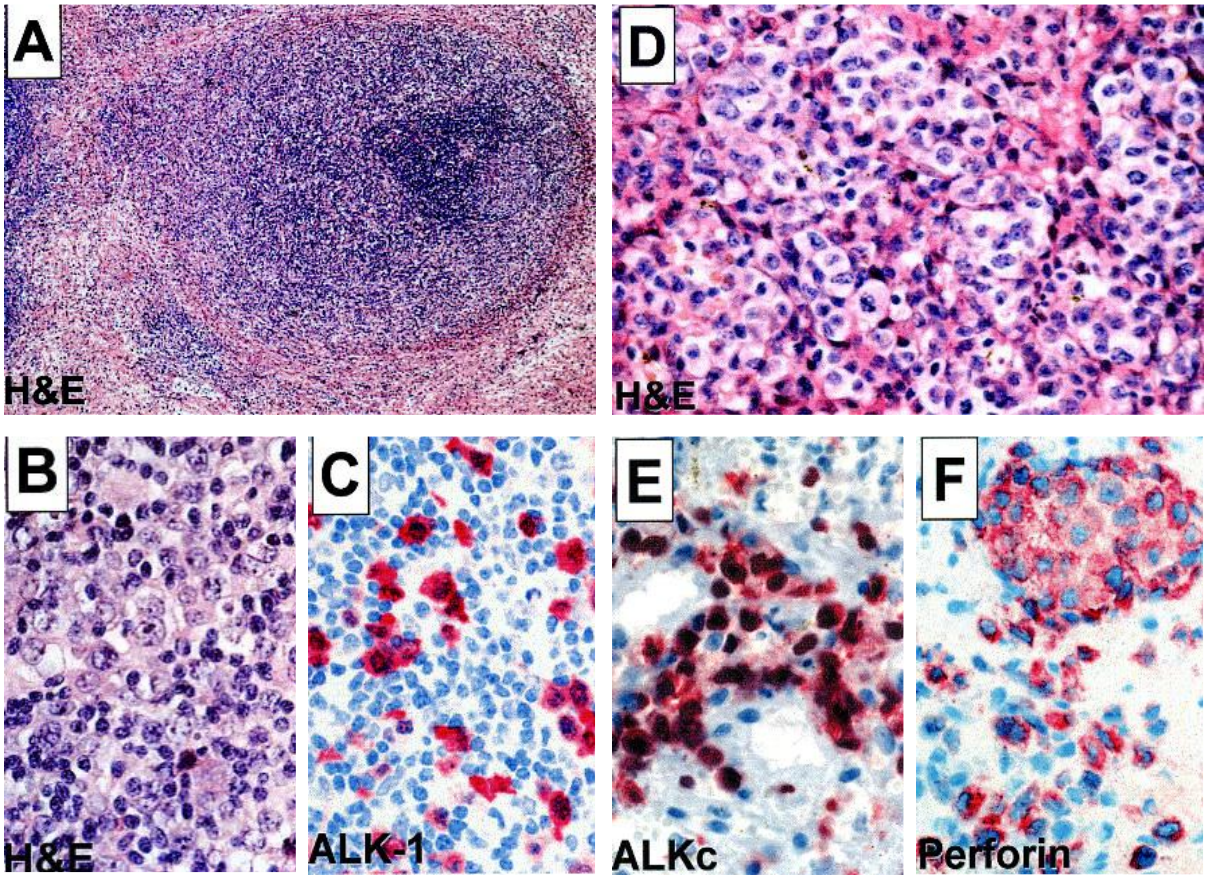

SCV
Mixed

(*Am J Surg Pathol* 2006;30:223–229)

ALK-Positive Anaplastic Large Cell Lymphoma Mimicking Nodular Sclerosis Hodgkin's Lymphoma

Report of 10 Cases

José Vassallo, MD, PhD,† Laurence Lamant, MD, PhD,* Laurence Brugieres, MD, PhD,‡ Fanny Gaillard, MD, PhD,§ Elias Campo, MD, PhD,‖ Pierre Brousset, MD, PhD,* and Georges Delsol, MD**



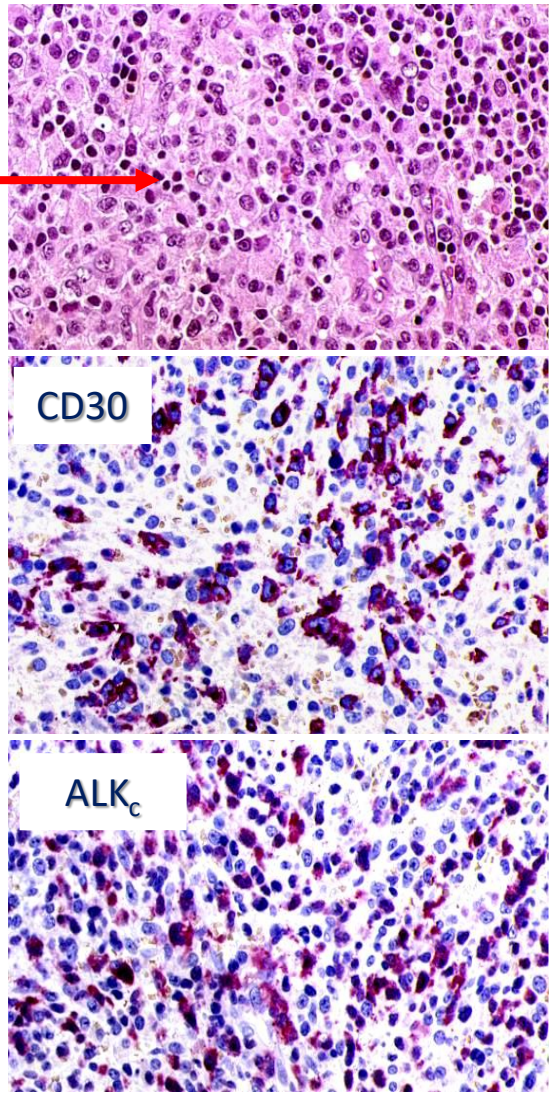
Further histological variants:

signet-ring cell[1],

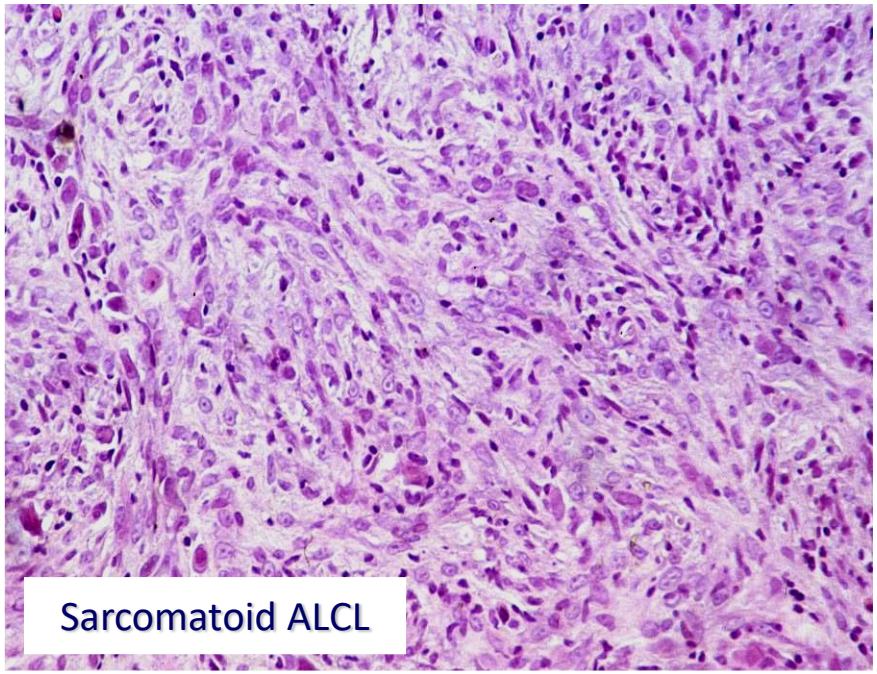
sarcomatoid[2-3],

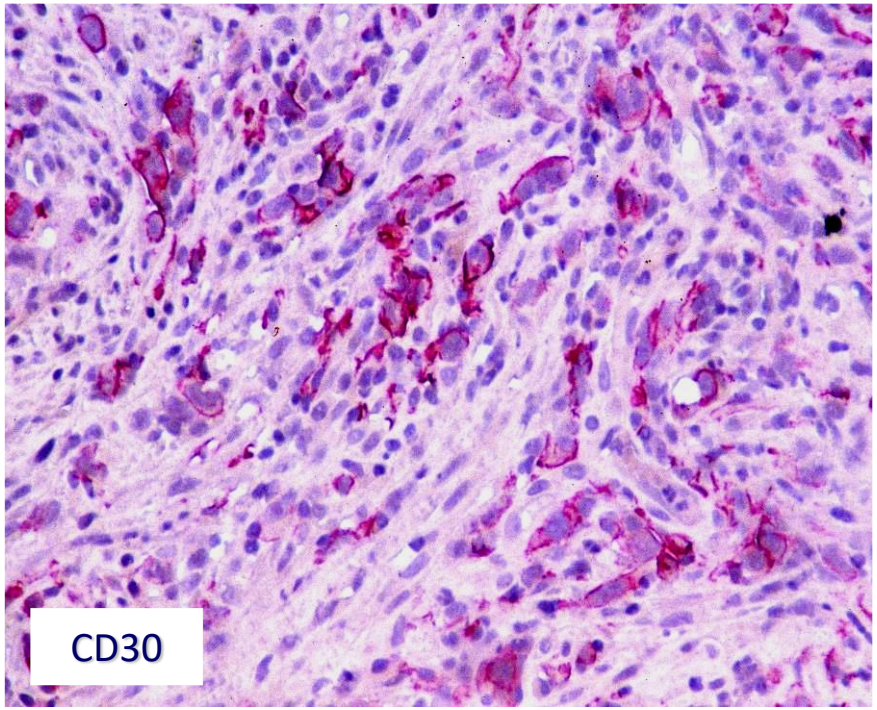
eosinophil-rich[4],

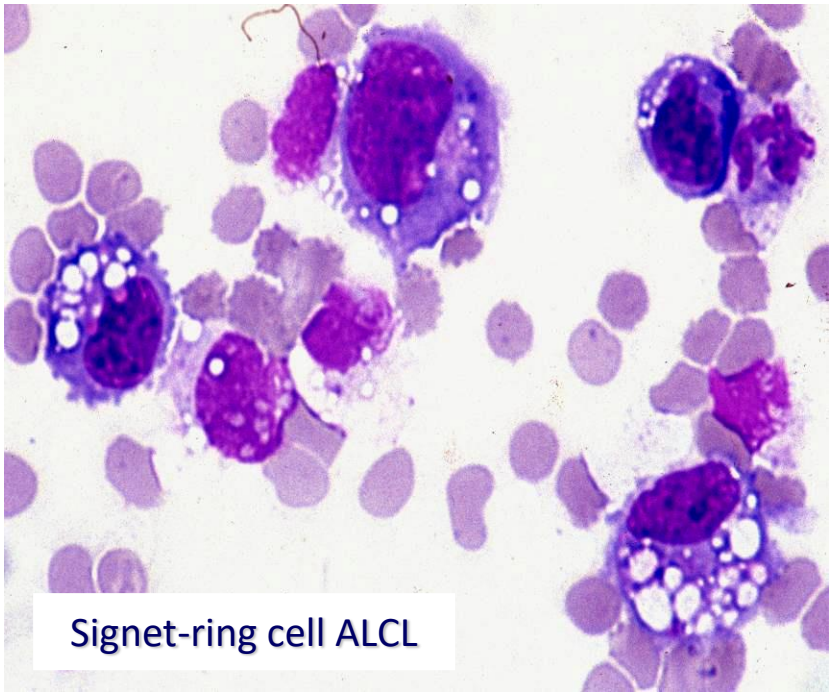
epithelioid cell-rich[5].

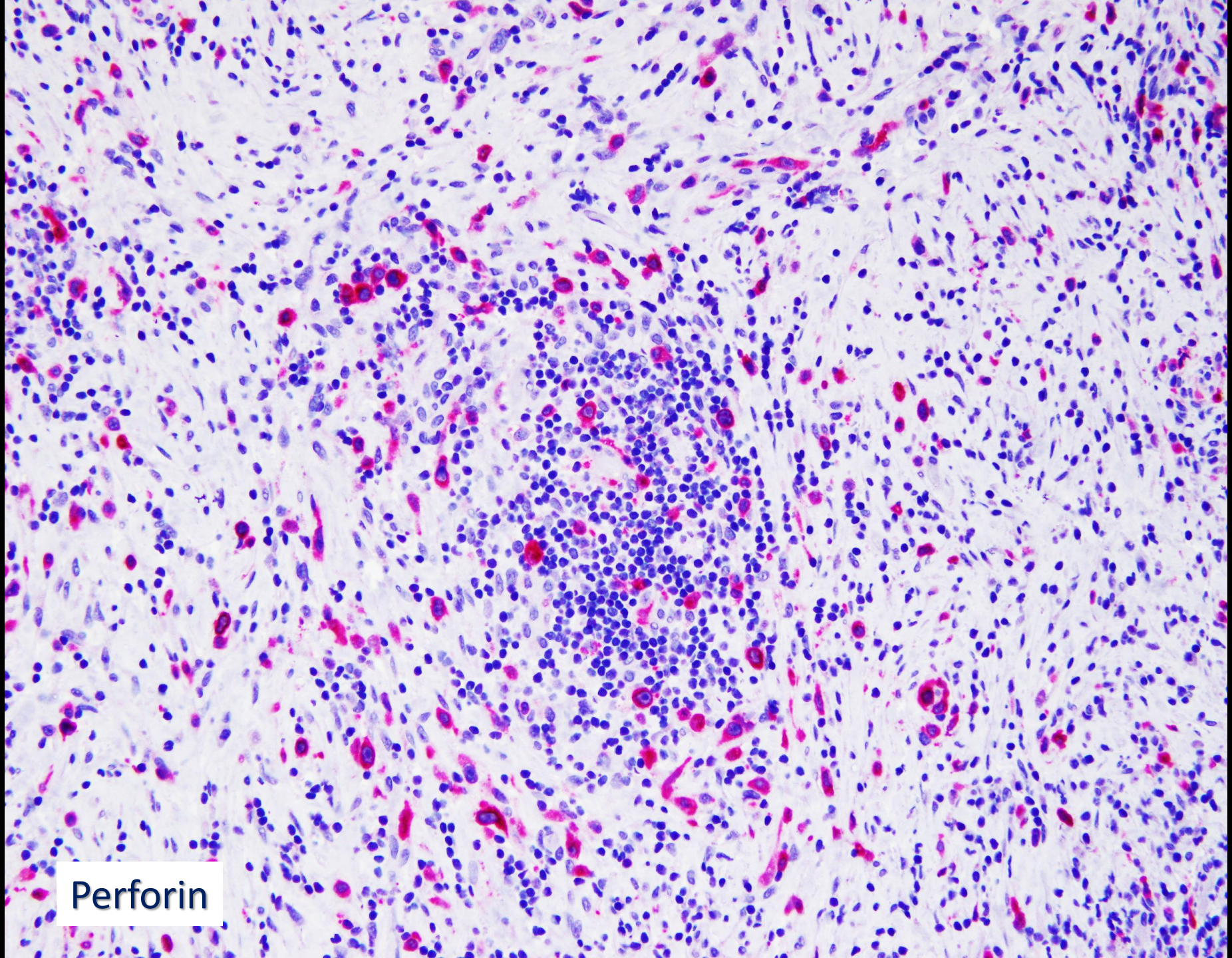


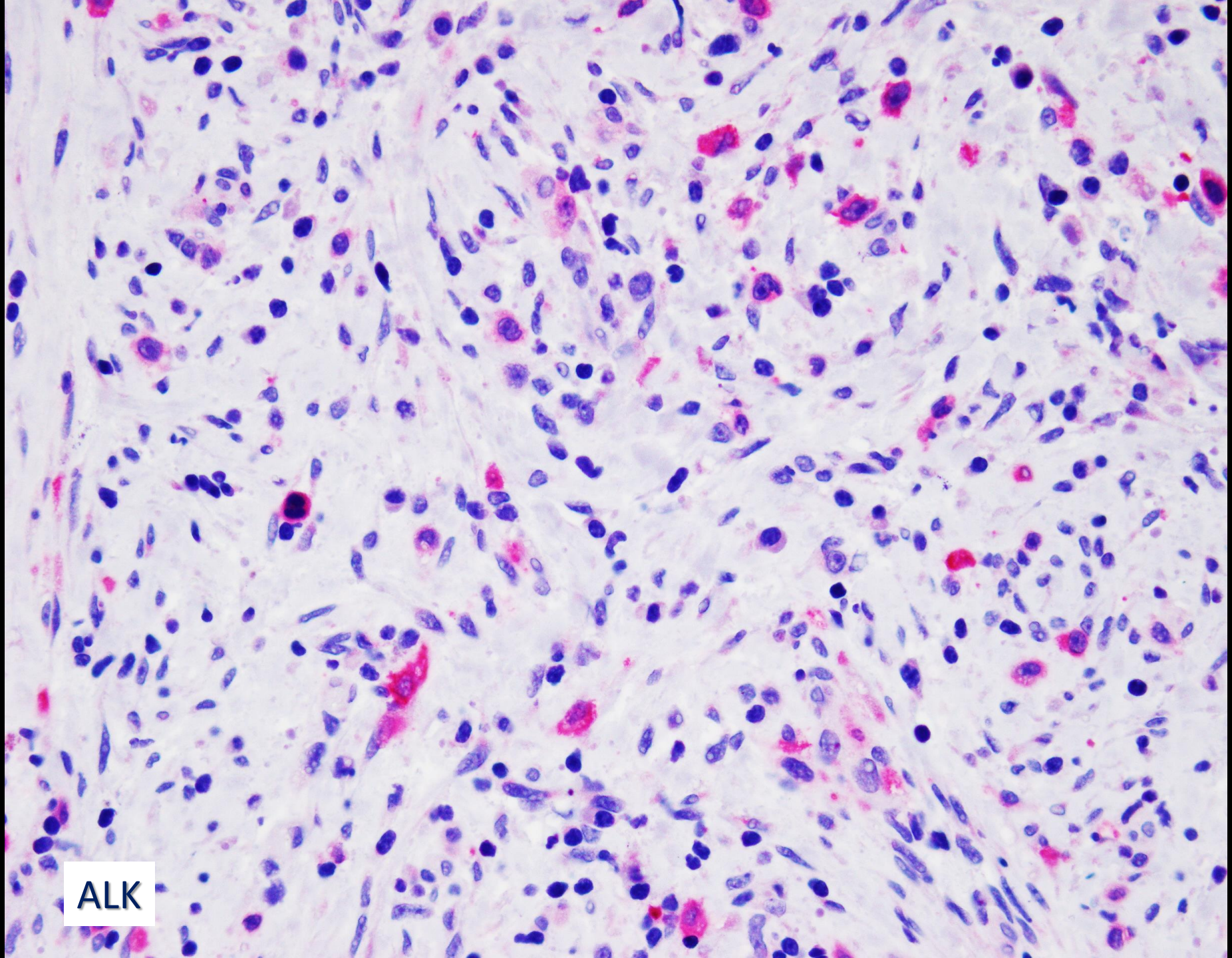
References: 1) Falini et al, Histopathol, 1997; 2) Bueso-Ramos et al, Mod Pathol, 1994; 3) Pereira et al, Arch Pathol Lab Med 2002; 4) McCluggage et al, Histopathol, 1998; 5) Piccaluga et al, Haematologica, 2000.

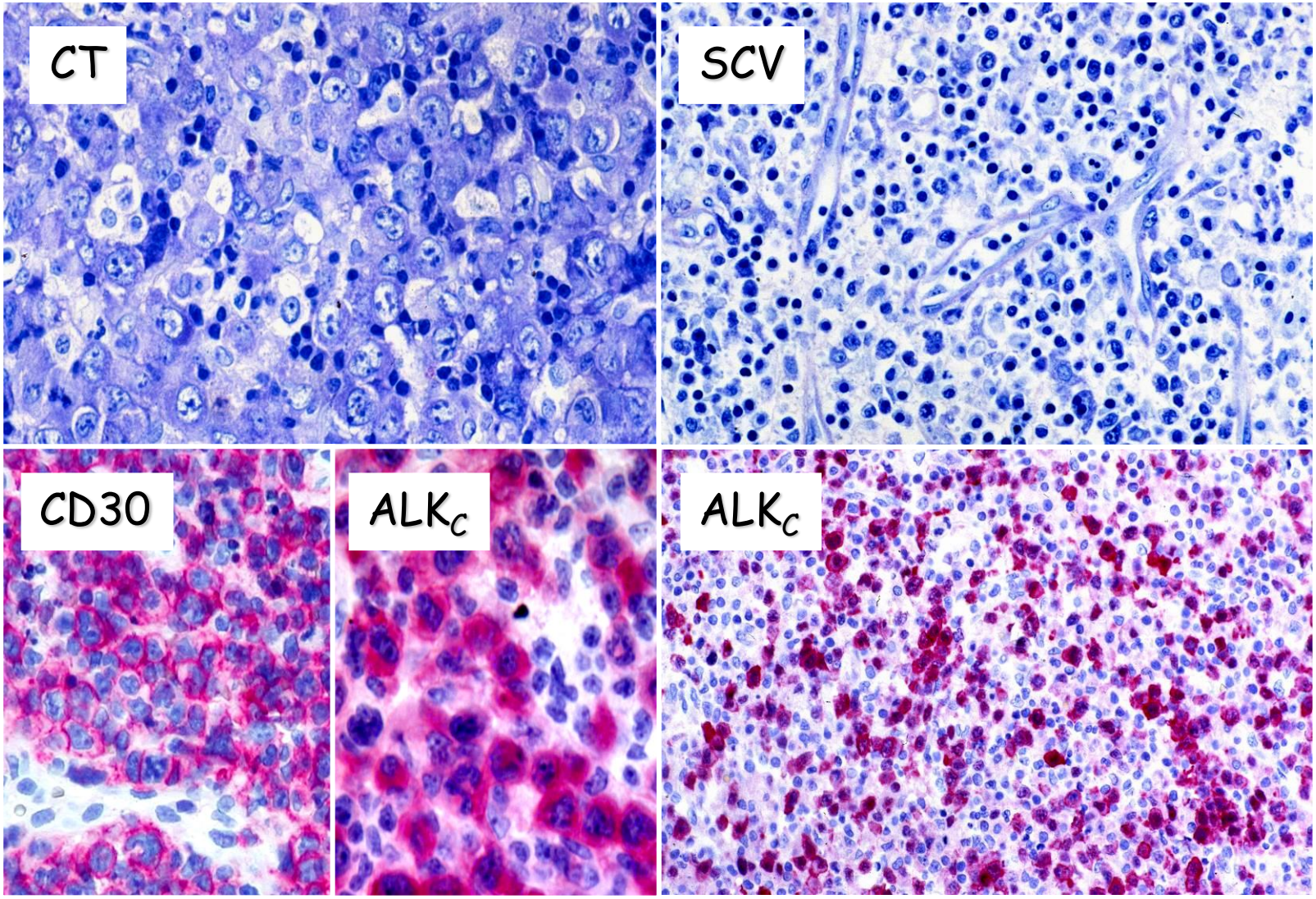

Sarcomatoid ALCL


CD30


Signet-ring cell ALCL


Perforin

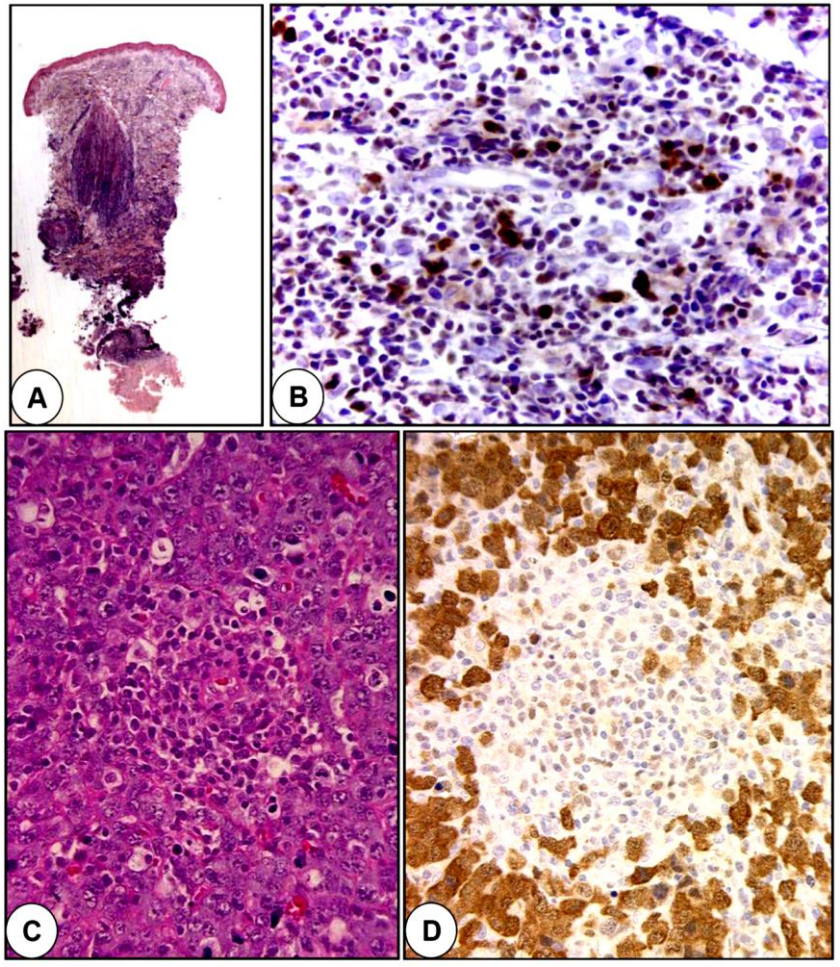

ALK


CT
SCV
CD30
ALK$_C$
ALK$_C$
Onset
Relapse

Cutaneous presentation of ALK-positive anaplastic large cell lymphoma following insect bites: evidence for an association in 5 cases.

L Lamant, S Pileri, E Sabattini, L Brugières, ES Jaffe and G Delsol

Haematologica 2010, 95:449-55.



Leukemia (2016), 1–4

www.nature.com/leu

LETTER TO THE EDITOR

NPM-ALK expression levels identify two distinct subtypes of paediatric anaplastic large cell lymphoma

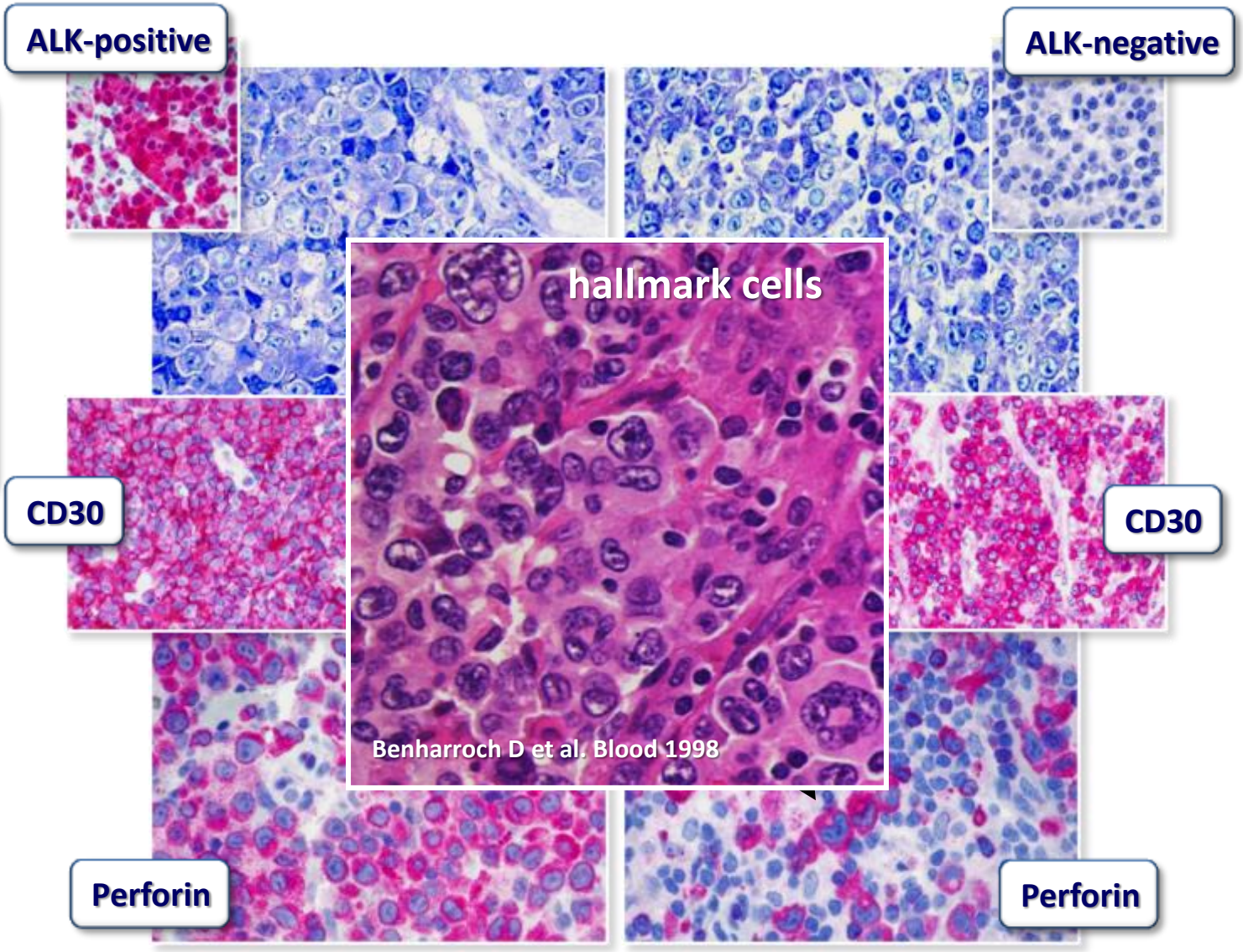
Anaplastic large cell lymphoma, ALK positive

Anaplastic large cell lymphoma, ALK negative
(UPGRADED TO DEFINITE ENTITY)

Breast implant-associated ALCL
(NEW PROVISIONAL ENTITY)

Anaplastic large cell lymphoma

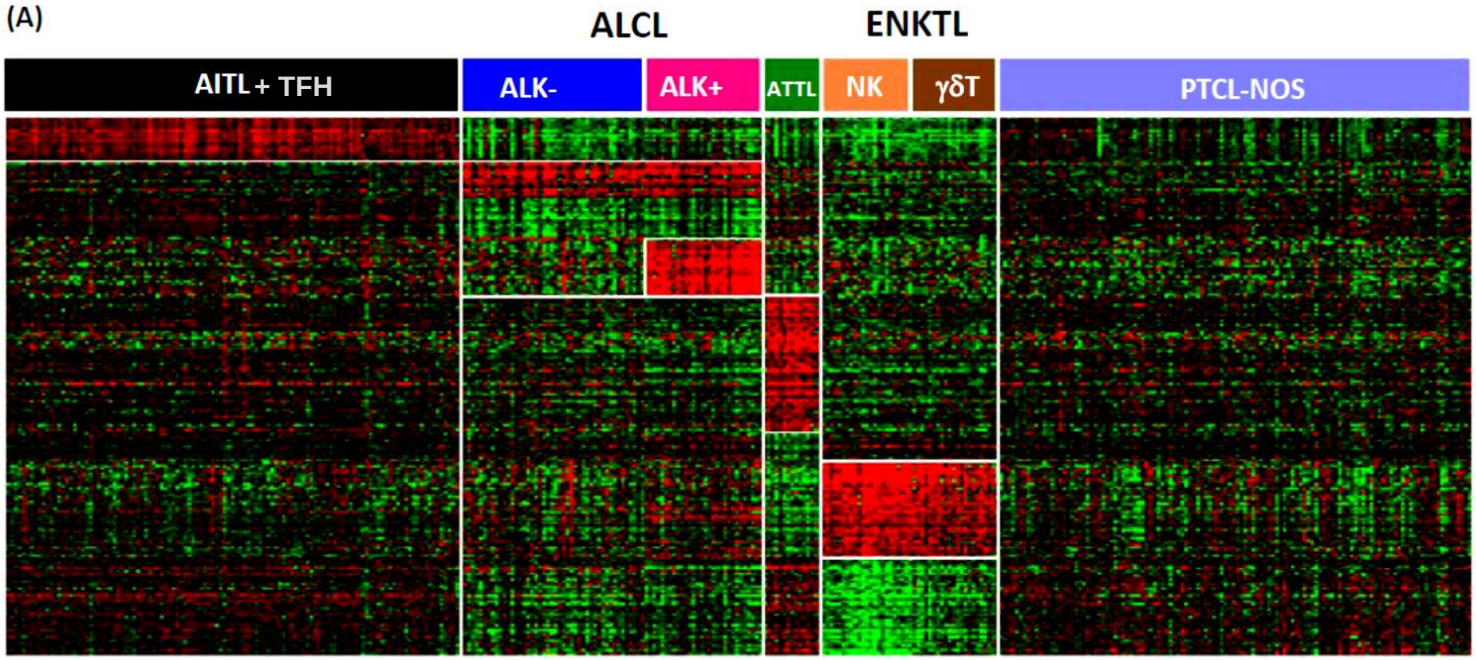
CD45+/-
EMA +/-
TCM -/+
CD43 +
CM +
PAX5 –
TCR/R



Gene expression signatures delineate biologic and prognostic subgroups in peripheral T-cell lymphoma

Javeed Iqbal, George Wright, Chao Wang, Andreas Rosenwald, Randy D. Gascoyne, Dennis D. Weisenburger, Timothy C. Greiner, Lynette Smith, Shuangping Guo, Ryan A. Wilcox, Bin Tean Teh, Soon Thye Lim, Soon Yong Tan, Lisa M. Rimsza, Elaine S. Jaffe, Elias Campo, Antonio Martinez, Jan Delabie, Rita M. Braziel, James R. Cook, Raymond R. Tubbs, German Ott, Eva Geissinger, Philippe Gaulard, Pier Paolo Piccaluga, Stefano A. Pileri, Wing Y. Au, Shigeo Nakamura, Masao Seto, Francoise Berger, Laurence de Leval, Joseph M. Connors, James Armitage, Julie Vose, Wing C. Chan and Louis M. Staudt

Prepublished online March 14, 2014;
doi:10.1182/blood-2013-11-536359



Convergent Mutations and Kinase Fusions Lead to Oncogenic STAT3 Activation in Anaplastic Large Cell Lymphoma

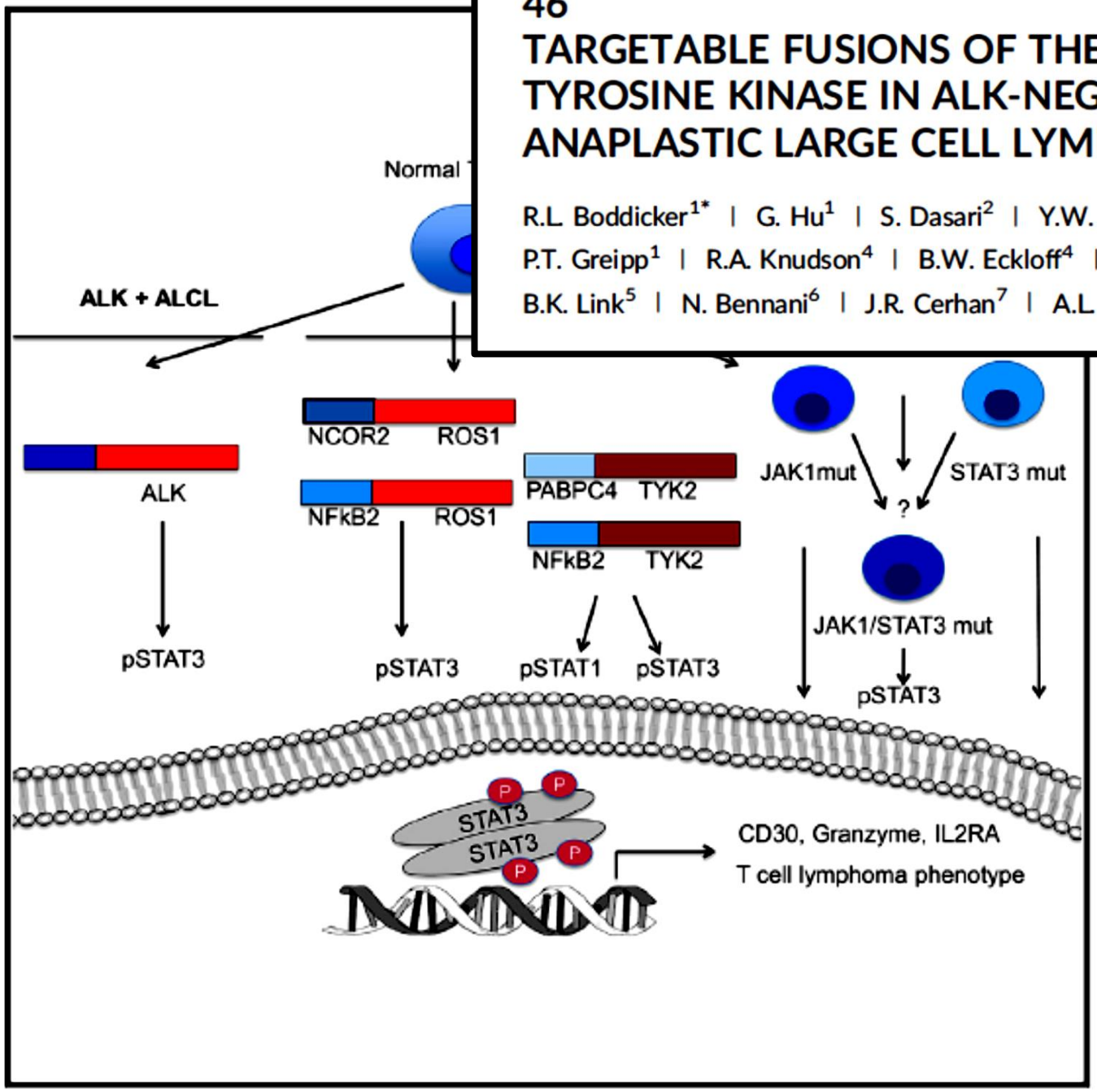
Ramona Crescenzo,[1,2,27] Francesco Abate,[1,3,4,27] Elena Lasorsa,[1,27] Fabrizio Tabbo',[1,2] Marcello Gaudiano,[1,2] Nicoletta Chiesa,[1] Filomena Di Giacomo,[1] Elisa Spaccarotella,[1] Luigi Barbarossa,[1] Elisabetta Ercole,[1] Maria Todaro,[1,2] Michela Boi,[1,2] Andrea Acquaviva,[3] Elisa Ficarra,[3] Domenico Novero,[5] Andrea Rinaldi,[6] Thomas Tousseyn,[7] Andreas Rosenwald,[8] Lukas Kenner,[9] Lorenzo Cerroni,[10] Alexander Tzankov,[11] Maurilio Ponzoni,[12] Marco Paulli,[13] Dennis Weisenburger,[14] Wing C. Chan,[14] Javeed Iqbal,[15] Miguel A. Piris,[16] Alberto Zamo',[17] Carmela Ciardullo,[18] Davide Rossi,[18] Gianluca Gaidano,[18] Stefano Pileri,[19,20] Enrico Tiacci,[21] Brunangelo Falini,[21] Leonard D. Shultz,[22] Laurence Mevellec,[23] Jorge E. Vialard,[24] Roberto Piva,[1,25] Francesco Bertoni,[6,26] Raul Rabadan,[4,*] Giorgio Inghirami,[1,2,25,*] and The European T-Cell Lymphoma Study Group, T-Cell Project: Prospective Collection of Data in Patients with Peripheral T-Cell Lymphoma and the AIRC 5xMille Consortium "Genetics-Driven Targeted Management of Lymphoid Malignancies"

516 Cancer Cell 27, 516–532, April 13, 2015

A systematic characterization of the genetic alterations driving ALCLs has not been performed. By integrating massive sequencing strategies, we provide a comprehensive characterization of driver genetic alterations (somatic point mutations, copy number alterations, and gene fusions) in ALK$^-$ ALCLs. We identified activating mutations of *JAK1* and/or *STAT3* genes in ~20% of 155 ALK$^-$ ALCLs and demonstrated that 38% of systemic ALK$^-$ ALCLs displayed double lesions. Recurrent chimeras combining a transcription factor (*NFkB2* or *NCOR2*) with a tyrosine kinase (*ROS1* or *TYK2*) were also discovered in WT JAK1/STAT3 ALK$^-$ ALCL. All these aberrations lead to the constitutive activation of the JAK/STAT3 pathway, which was proved oncogenic. Consistently, JAK/STAT3 pathway inhibition impaired cell growth in vitro and in vivo.

46
TARGETABLE FUSIONS OF THE FRK TYROSINE KINASE IN ALK-NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA

R.L. Boddicker[1*] | G. Hu[1] | S. Dasari[2] | Y.W. Asmann[3] | P.T. Greipp[1] | R.A. Knudson[4] | B.W. Eckloff[4] | J. Jen[1] | B.K. Link[5] | N. Bennani[6] | J.R. Cerhan[7] | A.L. Feldman[1]



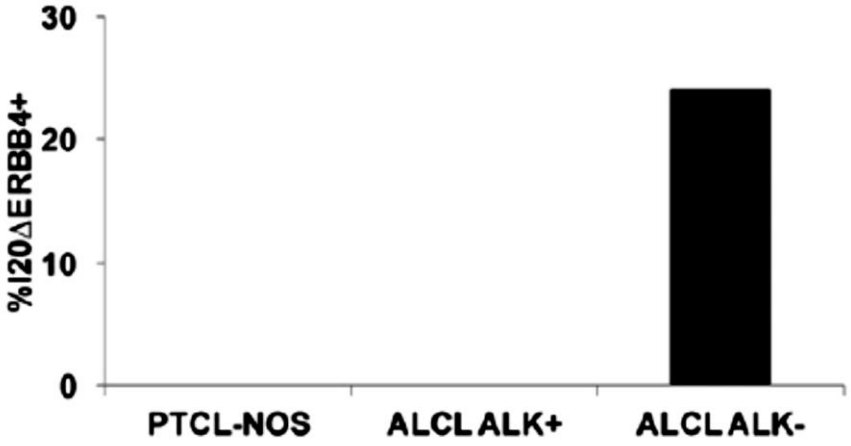
Identification of a new subclass of ALK-negative ALCL expressing aberrant levels of ERBB4 transcripts

(*Blood*. 2016;127(2):221-232)

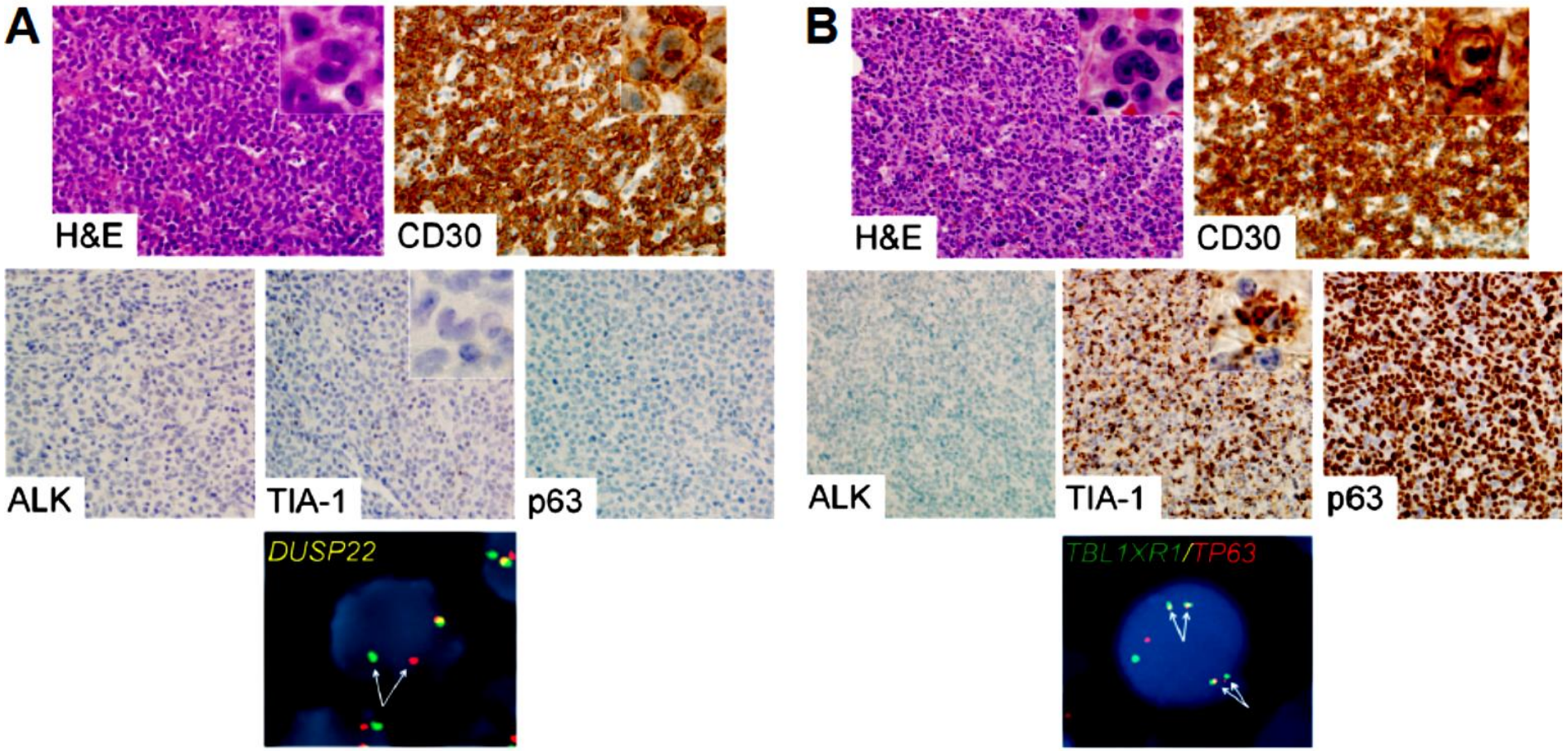
Irene Scarfò,[1,*] Elisa Pellegrino,[1,*] Elisabetta Mereu,[1,*] Ivo Kwee,[2-4] Luca Agnelli,[5,6] Elisa Bergaggio,[1] Giulia Garaffo,[1] Nicoletta Vitale,[1] Manuel Caputo,[1] Rodolfo Machiorlatti,[1] Paola Circosta,[1] Francesco Abate,[7] Antonella Barreca,[8] Domenico Novero,[8] Susan Mathew,[9] Andrea Rinaldi,[2] Enrico Tiacci,[10] Sara Serra,[11,12] Silvia Deaglio,[11,12] Antonino Neri,[5,6] Brunangelo Falini,[10] Raul Rabadan,[7] Francesco Bertoni,[2,13] Giorgio Inghirami,[1,9] Roberto Piva,[1,14] and the European T-Cell Lymphoma Study Group

Key Points

- Endogenous intronic long terminal repeats promote the ectopic expression of truncated ERBB4 transcripts in 24% of ALK-negative ALCL.
- The expression of ERBB4-aberrant transcripts defines a new subclass of ALK-negative ALCL and may contribute to ALCL transformation.



	Samples	I20ΔERBB4+	%I20ΔERBB4+
PTCL-NOS	51	0	0
ALCL ALK+	44	0	0
ALCL ALK-	75	18	24
tot	170		


A
H&E
CD30
ALK
TIA-1
p63
DUSP22
B
H&E
CD30
ALK
TIA-1
p63
TBL1XR1/TP63

Expression of p63 protein in anaplastic large cell lymphoma: implications for genetic subtyping☆,☆☆

Xueju Wang MD, PhD[a,b,1], Rebecca L. Boddicker PhD[a,1], Surendra Dasari PhD[c], Jagmohan S. Sidhu MD[d], Marshall E. Kadin MD[e], William R. Macon MD[a], Stephen M. Ansell MD, PhD[f], Rhett P. Ketterling MD[a], Karen L. Rech MD[a], Andrew L. Feldman MD[a,*]

Human Pathology (2017) **64**, 19–27

Summary Anaplastic large cell lymphomas (ALCLs) are CD30-positive T-cell non-Hodgkin lymphomas that bear chromosomal rearrangements of the *TP53* homologue *TP63* in a subset of cases that demonstrate aggressive clinical behavior. In the present study, we examined the relationship between p63 protein expression by immunohistochemistry and the results of fluorescence in situ hybridization using *TP63* probes in 116 ALCLs. We also determined the relative expression of full-length TAp63 and truncated ΔNp63 isoforms (eg, p40) in ALCL cell lines and a subset of clinical cases. Overall, 35.3% of ALCLs were positive for p63 protein. Primary cutaneous and anaplastic lymphoma kinase–negative ALCLs were positive more frequently than anaplastic lymphoma kinase–positive ALCLs ($P = .0034$). As previously reported, cases with *TP63* gene rearrangements expressed p63 uniformly. p63 expression in nonrearranged cases was associated with extra copies of *TP63* on 3q28 ($P < .0001$). Extra copies of *TP63* correlated with extra copies of the *DUSP22* locus on 6p25.3 ($P < .0001$). Results of immunohistochemistry, Western blotting, and RNA sequencing indicated that p63 expression in nonrearranged cases was entirely attributable to TAp63 isoforms. Taken together, these findings indicate that ALCLs without *TP63* rearrangements may express TAp63 isoforms of p63 and that this expression is associated with extra copies of *TP63*, probably due to widespread genomic copy number abnormalities rather than focal gains. Immunohistochemistry for p63 in ALCL is not specific for *TP63* rearrangements but is useful clinically as a screening test to select cases

Histopathology 2015, **66**, 846–855. DOI: 10.1111/his.12529

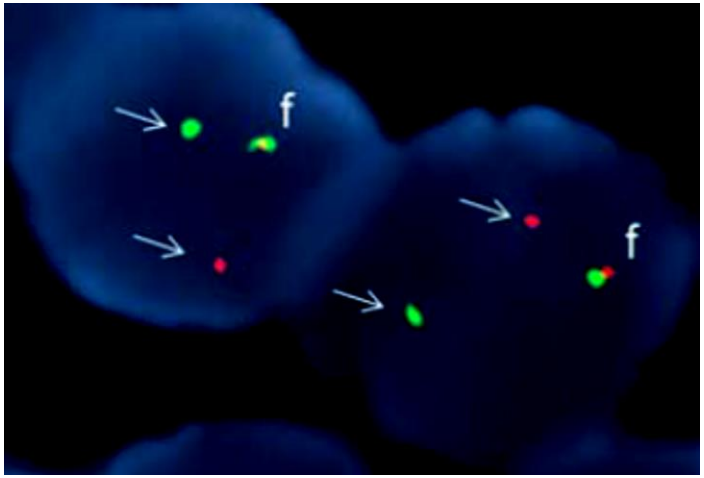
Primary cutaneous anaplastic large cell lymphomas with 6p25.3 rearrangement exhibit particular histological features

Arantza Onaindia,[1] Santiago Montes-Moreno,[1] Socorro M Rodríguez-Pinilla,[2] Ana Batlle,[3] Sonia González de Villambrosía,[3] Antonio M Rodríguez,[4] Víctor Alegre,[5] Glenda M Bermúdez,[1] Carmen González-Vela[1] & Miguel A Piris[1]

Chromosomal Rearrangements of 6p25.3 Define a New Subtype of Lymphomatoid Papulosis

Laszlo J. Karai, MD,† Marshall E. Kadin, MD,‡ Eric D. Hsi, MD,§ Jason C. Sluzevich, MD,‖ Rhett P. Ketterling, MD,¶ Ryan A. Knudson, BS,¶ and Andrew L. Feldman, MD¶*

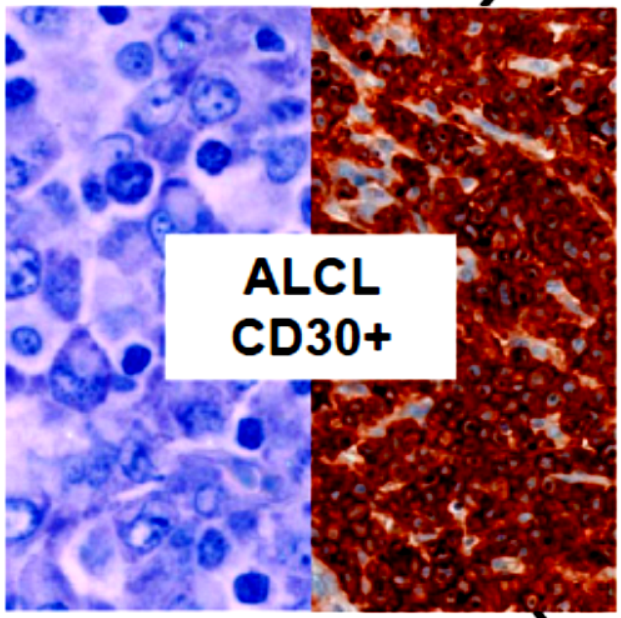
(*Am J Surg Pathol* 2013;37:1173–1181)



ALK^{-} ALCL with *DUSP22* rearrangement shows:

- lack of STAT3 activation,
- over-expression of immunogenic cancer-testis antigen genes,
- marked DNA hypomethylation,
- minimal expression of PD-L1,
- high expression of CD58 and HLA class II.

Courtesy of Dr. Andrew L. Feldman



ALK+

Systemic

100% *ALK* rearr.
STAT3 key effector

sALCL
ALK+

Systemic

Rearrangements: *IRF4/DUSP22*, *TP63*, tyrosine kinases,
Overexpresssion:ERBB4
Mutations: *JAK1/STAT3*

sALCL
ALK-

ALK-

Cutaneous

cALCL

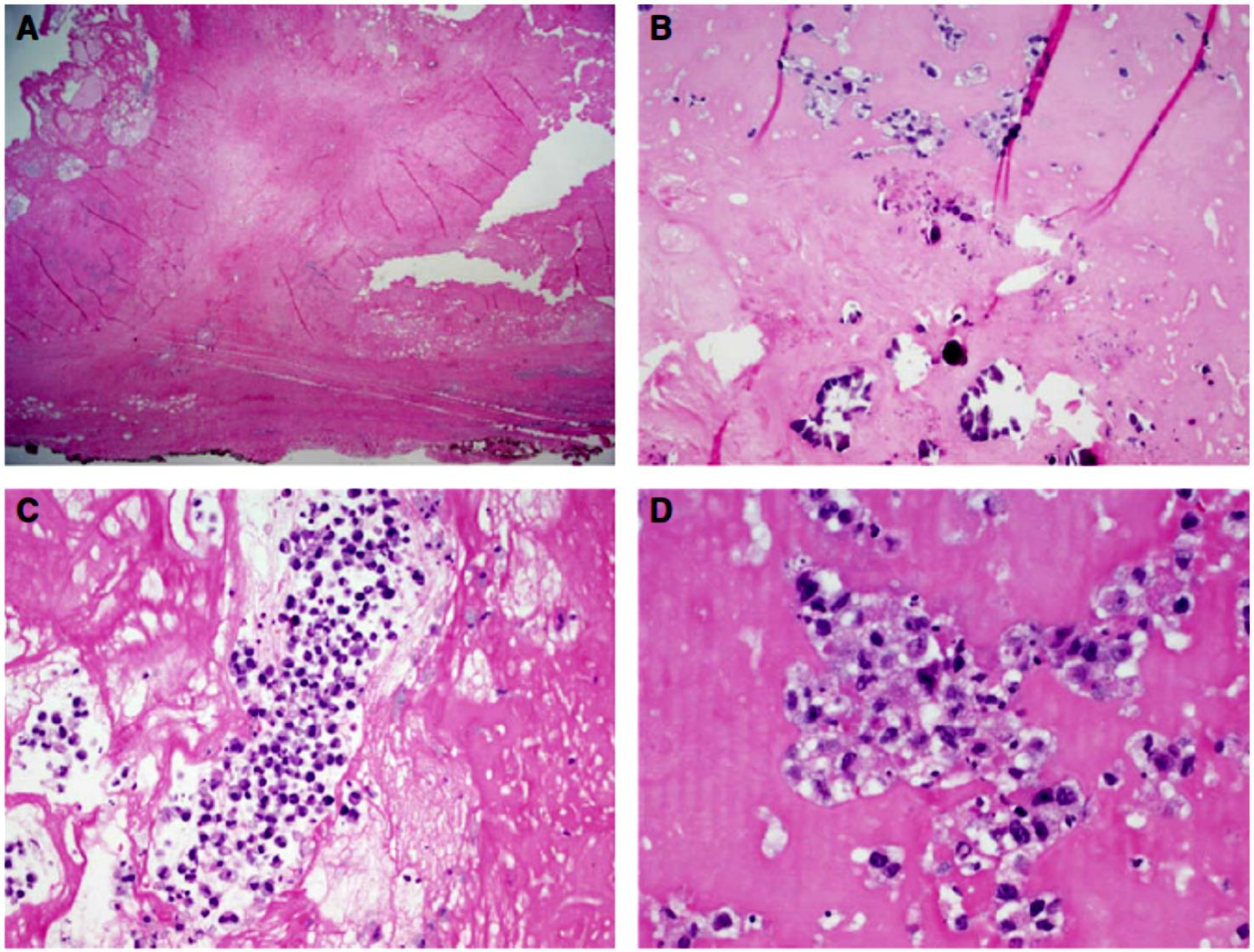
Anaplastic large cell lymphoma, ALK positive

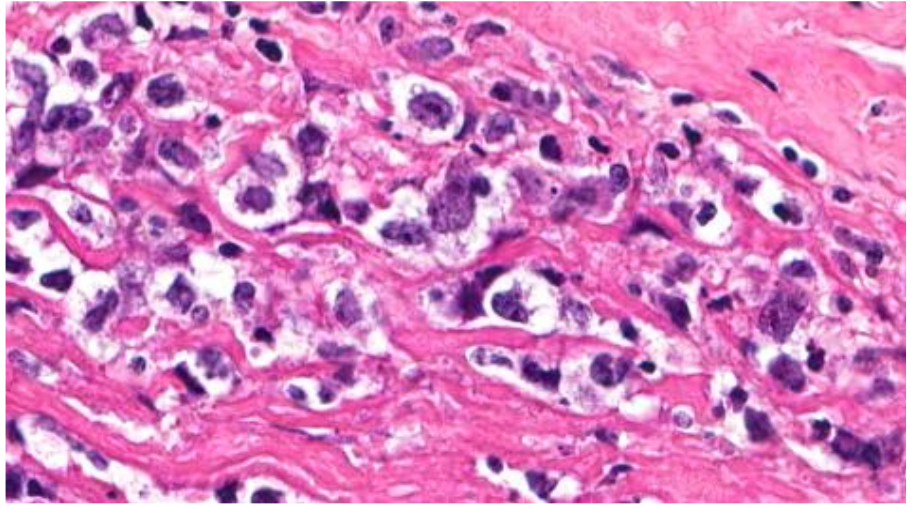
Anaplastic large cell lymphoma, ALK negative
(UPGRADED TO DEFINITE ENTITY)

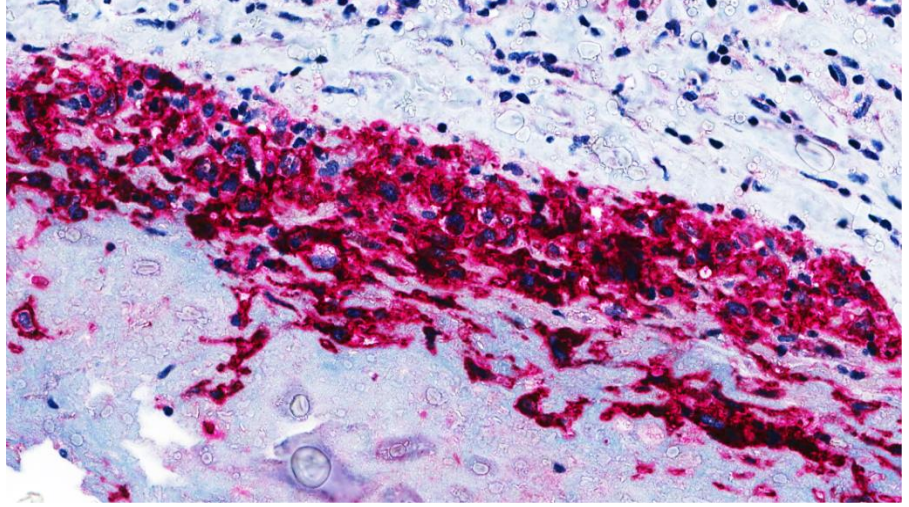
Breast implant-associated ALCL
(NEW PROVISIONAL ENTITY)

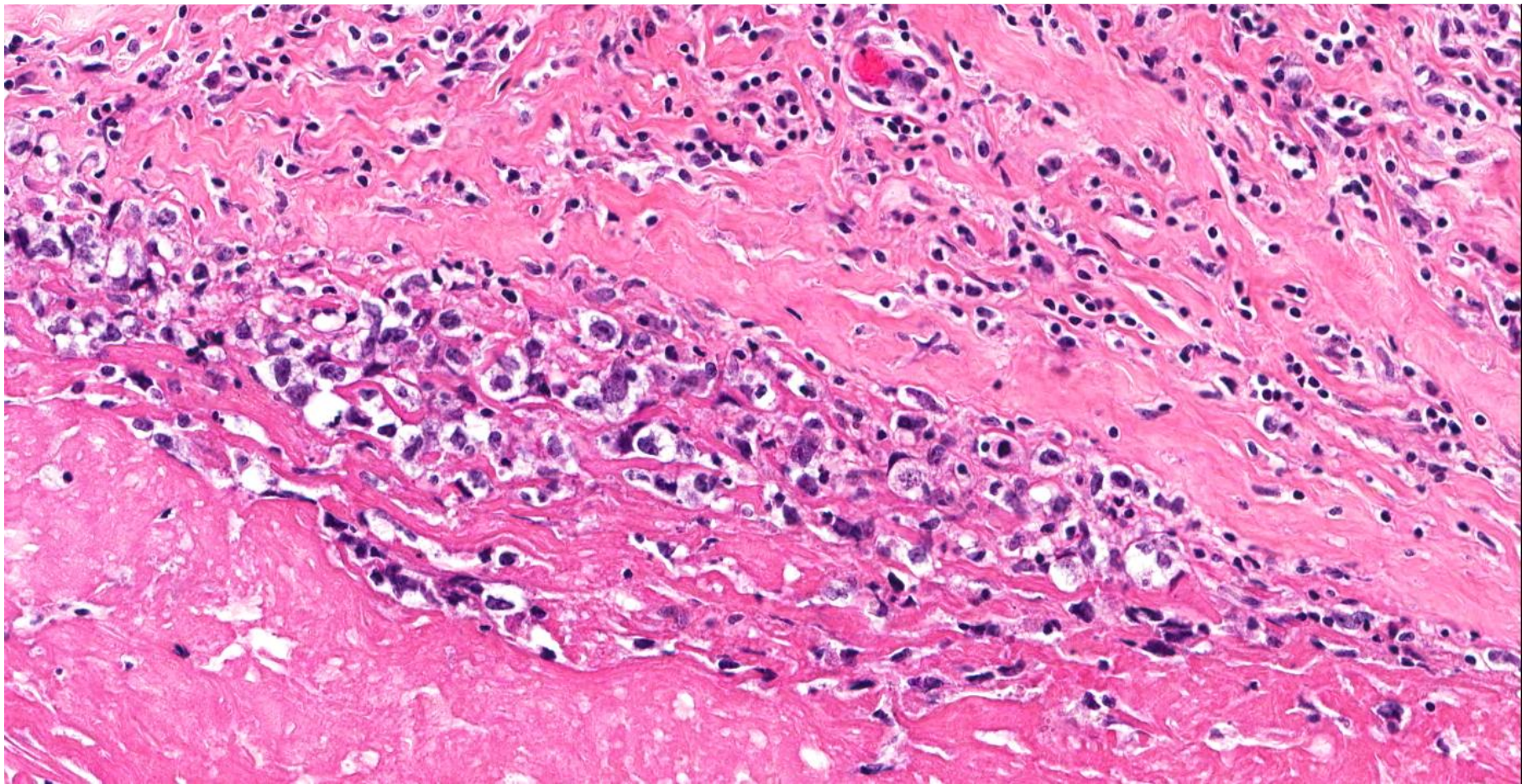
Seroma-associated anaplastic large-cell lymphoma arising on the background of subcutaneous calcinosis: beyond breast implants

Histopathology, 69, 883–897.









VOLUME 34 · NUMBER 2 · JANUARY 10, 2016

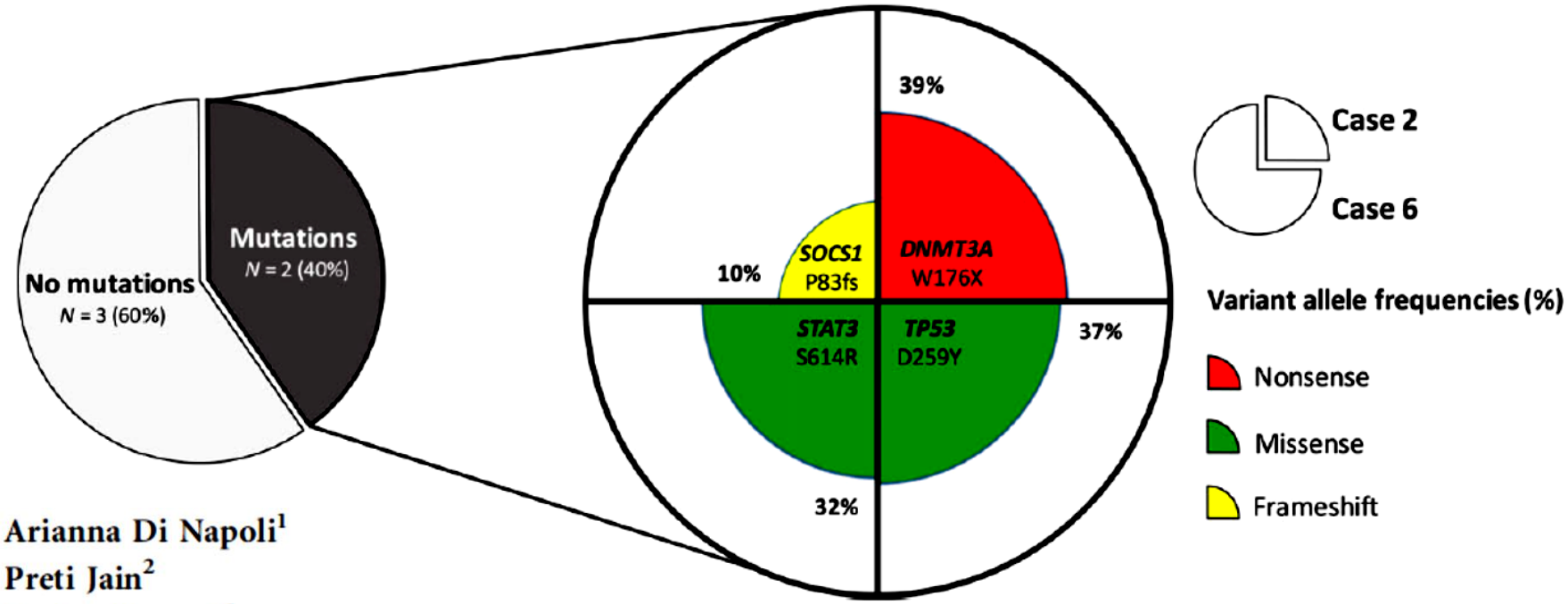
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Complete Surgical Excision Is Essential for the Management of Patients With Breast Implant–Associated Anaplastic Large-Cell Lymphoma

Mark W. Clemens, L. Jeffrey Medeiros, Charles E. Butler, Kelly K. Hunt, Michelle A. Fanale, Steven Horwitz, Dennis D. Weisenburger, Jun Liu, Elizabeth A. Morgan, Rashmi Kanagal-Shamanna, Vinita Parkash, Jing Ning, Aliyah R. Sohani, Judith A. Ferry, Neha Mehta-Shah, Ahmed Dogan, Hui Liu, Nora Thormann, Arianna Di Napoli, Stephen Lade, Jorge Piccolini, Ruben Reyes, Travis Williams, Colleen M. McCarthy, Summer E. Hanson, Loretta J. Nastoupil, Rakesh Gaur, Yasuhiro Oki, Ken H. Young, and Roberto N. Miranda

Targeted next generation sequencing of breast implant-associated anaplastic large cell lymphoma reveals mutations in JAK/STAT signalling pathway genes, *TP53* and *DNMT3A*



Arianna Di Napoli[1]
Preti Jain[2]
Enrico Duranti[1]
Elizabeth Margolskee[2]
Walter Arancio[3]
Fabio Facchetti[4]
Bachir Alobeid[2]
Fabio Santanelli di Pompeo[5]
Mahesh Mansukhani[2]
Govind Bhagat[2]


рахмат
danke
謝謝
ngiyabonga
spas
teşekkür ederim
Баярлалаа
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kia ora
barka
welalin
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mahalo
tapadh leat
спасибо
faafetai lava
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biagodaram
dank je
misaotra
paldies
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matondo
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thank you
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nanni
nandri
dhanyavad
mauruuru
хвала
asante
manana
bedankt
hvala
gracie
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koszonom
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