



Webinars

Cutaneous Lymphoma

EuroBloodNet  Topic on Focus

Primary cutaneous Large B-cell lymphoma, Leg-type

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French Study Group of Cutaneous Lymphoma (General secretary)

ERN-EuroBloodNet subnetwork Cutaneous Lymphomas

Bordeaux – France

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université
de BORDEAUX



BaRITON
Bordeaux Research
in Translational Oncology



European
Reference
Network

for rare or low prevalence
complex diseases

Network
Hematological
Diseases (ERN EuroBloodNet)



Research funding : Celgene, Roche

Advisory board member : Roche, Takeda, Kyowa,
Recordati

Principal Investigator : Celgene, Kyowa Hakko,
Millenium, Roche, Biocryst, ArgenX, 4SC, Galderma,
Miragen

The beginning of the story



Primary Cutaneous Large B-Cell Lymphomas of the Legs

A Distinct Type of Cutaneous B-Cell Lymphoma With an Intermediate Prognosis

Maarten H. Vermeer, MD; Françoise A. M. J. Geelen, MD; Chris W. van Haselen; Pieter C. van Voorst Vader, MD; Marie-Louise Geerts, MD; Willem A. van Vloten, MD; Rein Willemze

18 patients (med 76 years), MF ratio 7.2, legs 14/18; 5-y survival = 58%

Arch Dermatol. 1996;132(11):1304-1308. doi:10.1001/archderm.1996.03890350042008

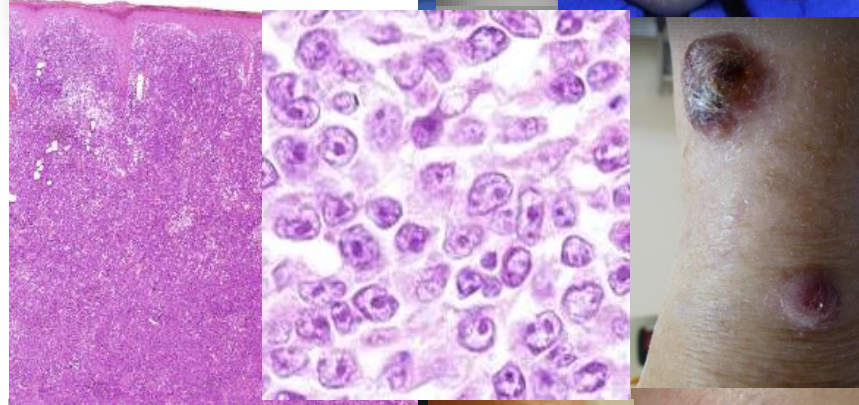


Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type

Arch Dermatol. 2007;143(9):1144-1150

Clinicopathologic Features and Prognostic Analysis in 60 Cases

Florent Grange, MD, PhD; Marie Beylot-Barry, MD, PhD; Phillippe Courville, MD; Eve Maubec, MD; Martine Bagot, MD, PhD; Béatrice Vergier, MD, PhD; Pierre Souteyrand, MD; Laurent Machet, MD, PhD; Sophie Dalac, MD; Eric Esteve, MD; Isabelle Templier, MD; Emmanuel Delaporte, MD; Marie-Françoise Avril, MD; Caroline Robert, MD, PhD; Stephane Dalle, MD; Liliane Laroche, MD, PhD; Michele Delaunay, MD; Pascal Joly, MD, PhD; Janine Wechsler, MD; Tony Petrella, MD



Mean age 76 years, Leg 72%; 5-year survival = 41%

Prognostic factors : age, multiple lesions, leg localisation, ulceration



A very suggestive clinical presentation



- **82-year old woman**
- **Tumor of the right leg appeared in 2 months**
- **No other skin lesions**
- **No adenopathy**
- **Good general condition (ECOG = 0)**

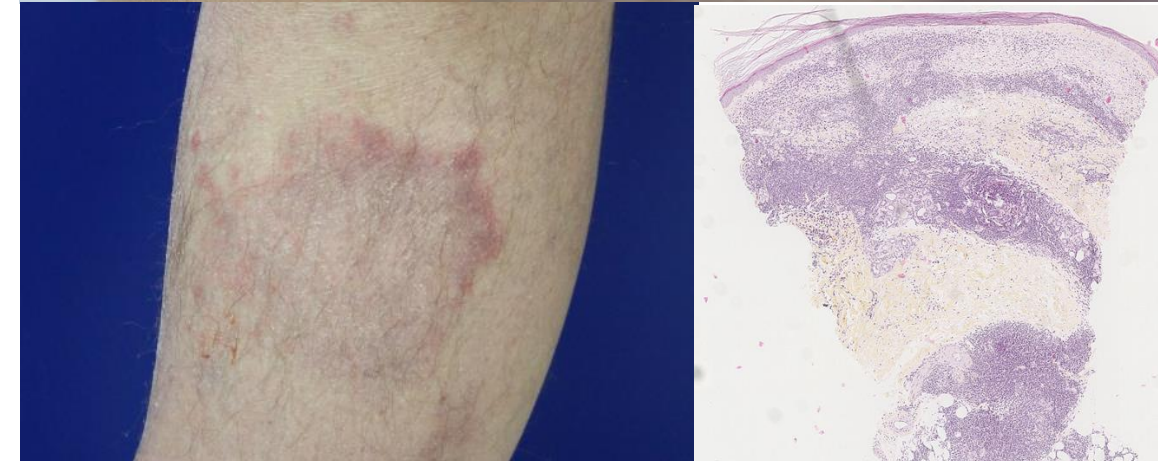


Some unusual presentations

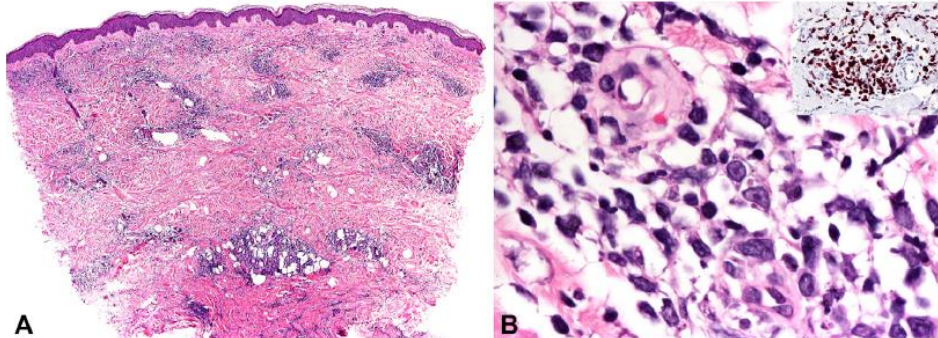
J AM ACAD DERMATOL
JUNE 2015

Atypical clinicopathologic presentation of primary cutaneous diffuse large B-cell lymphoma, leg type

Cesare Massone, MD, Regina Fink-Puches, MD, Ingrid Wolf, MD, Iris Zalaudek, MD, and Lorenzo Cerroni, MD
Graz, Austria

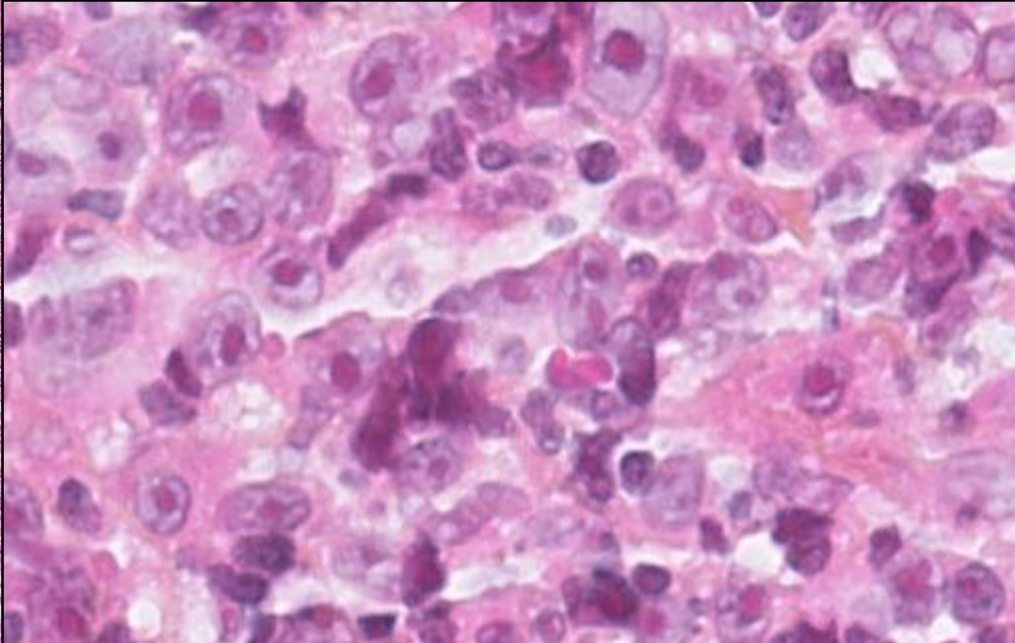
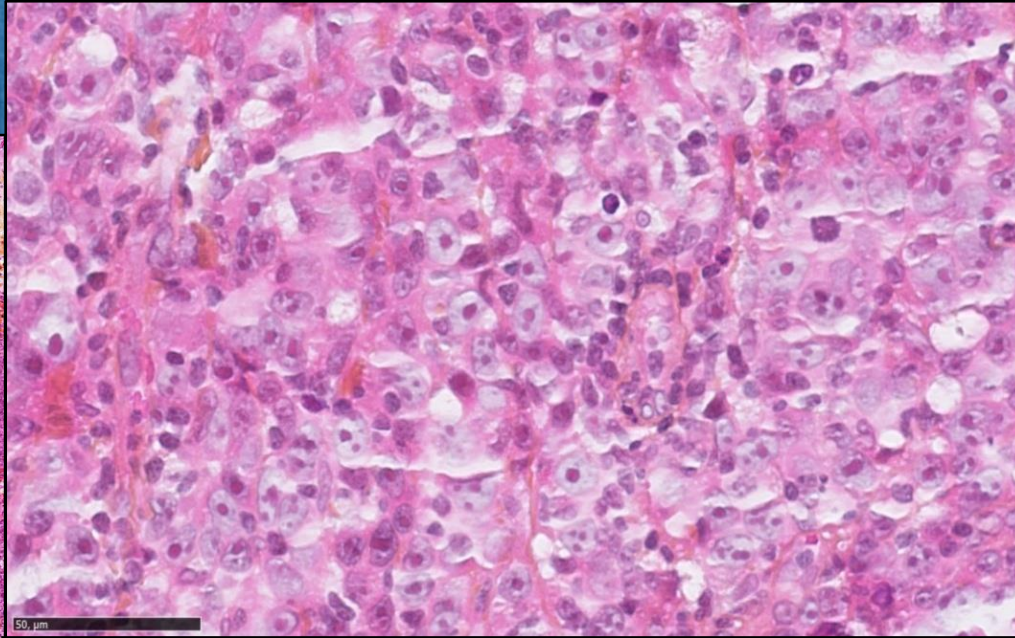
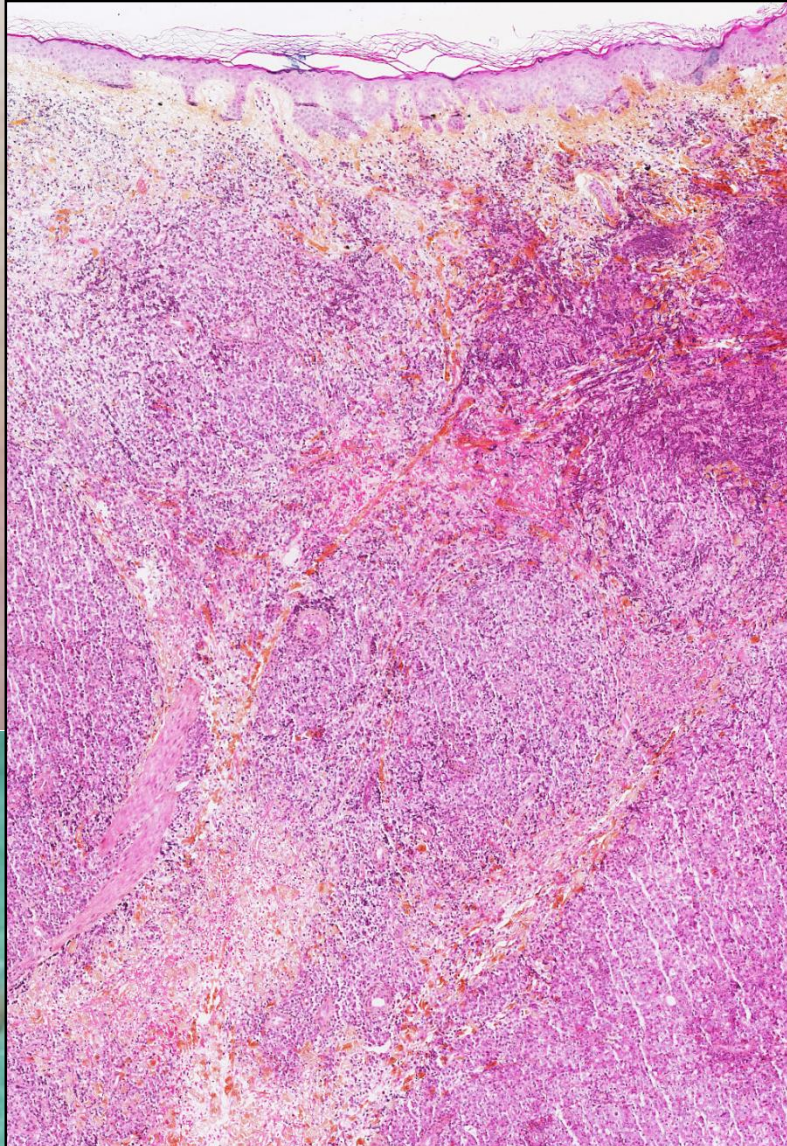


Personal cases



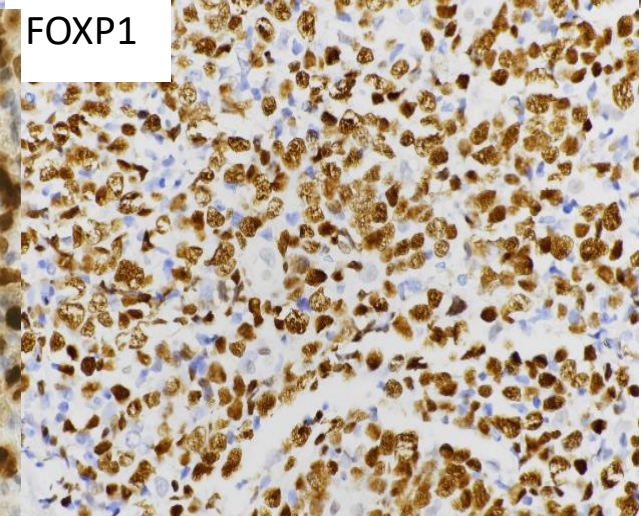
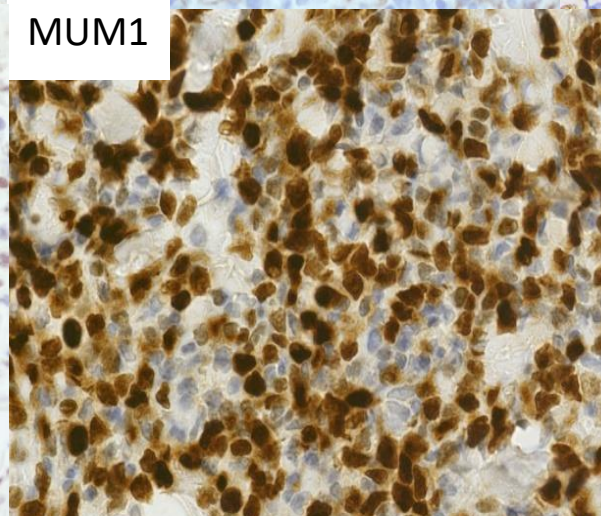
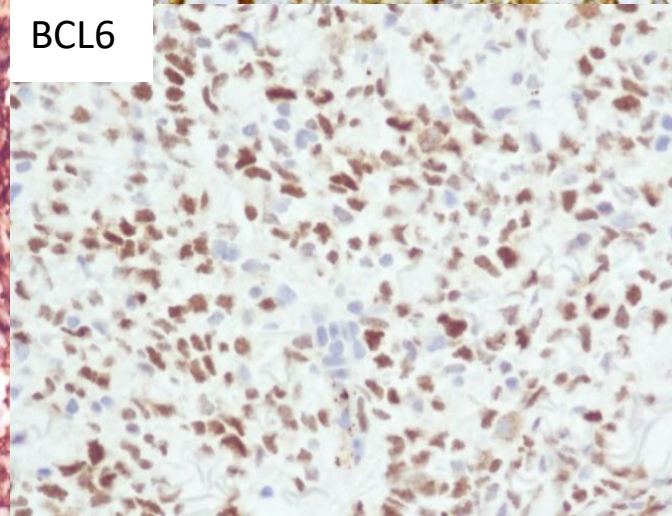
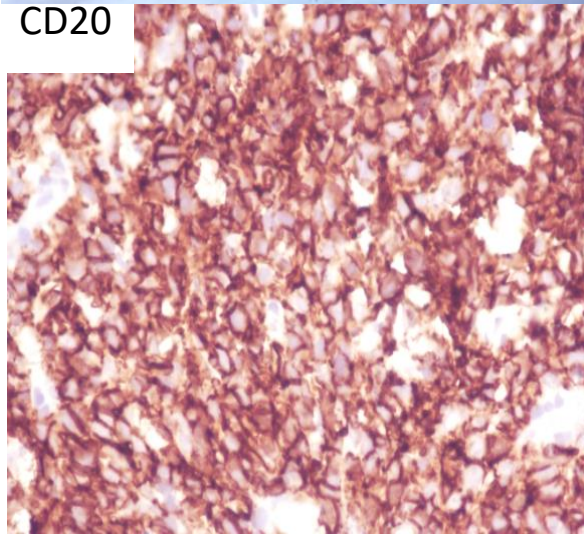
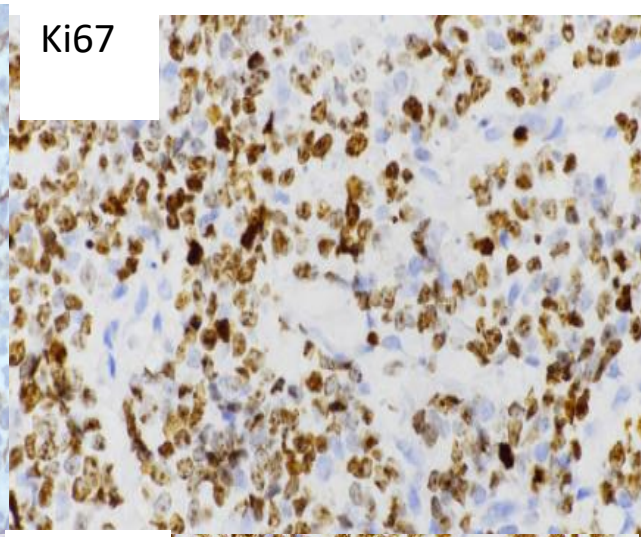
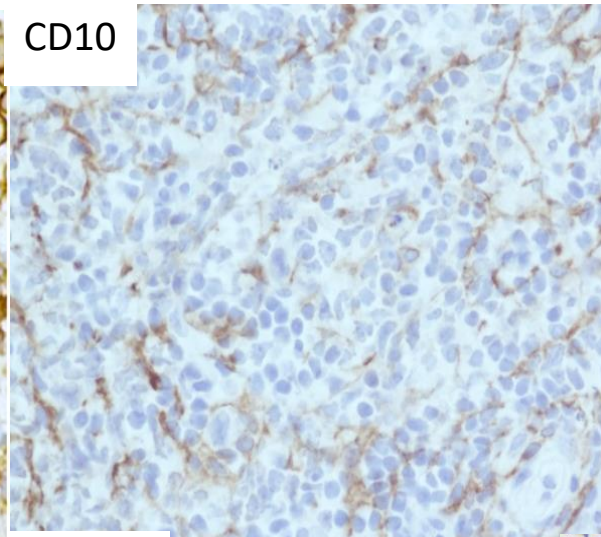
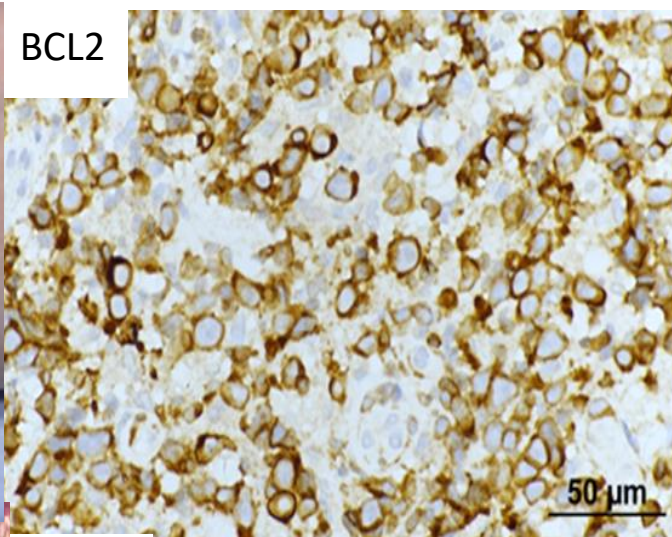
A

B

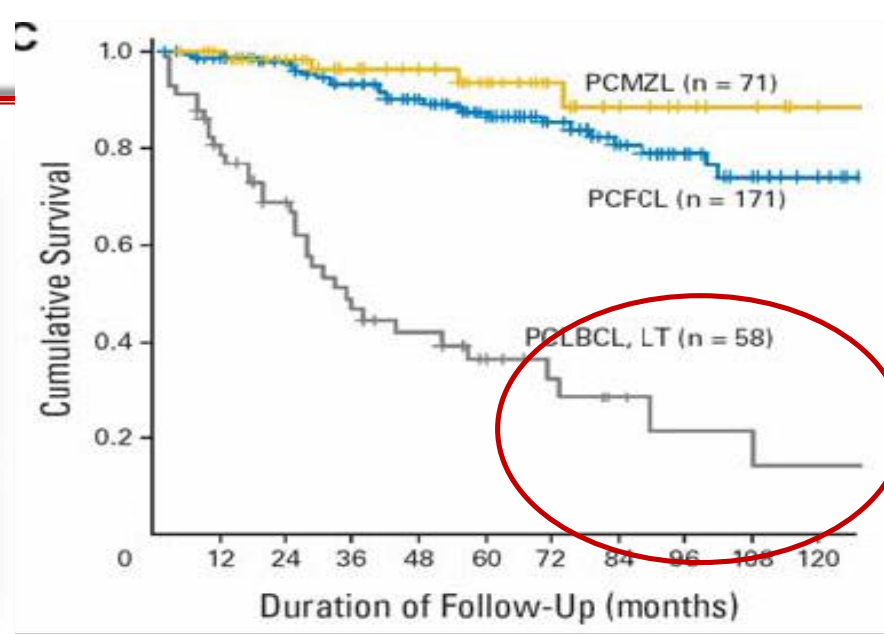
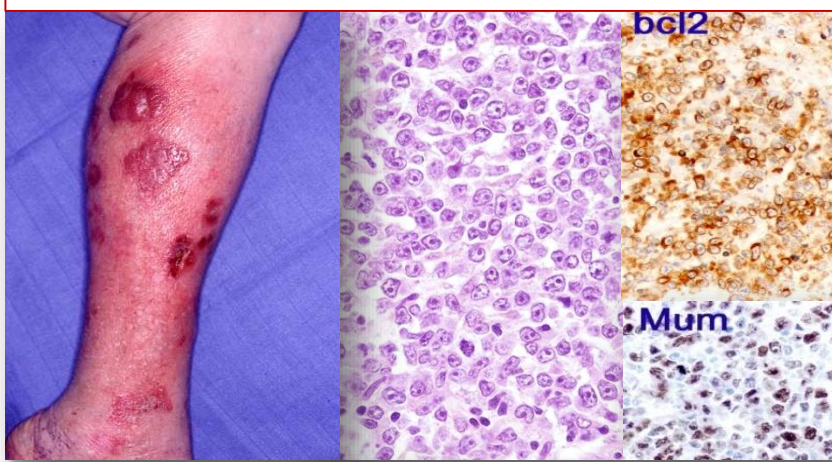




Expression profile: BCL2+ MUM1+, FOXP1+, BCL6+/-, CD10-

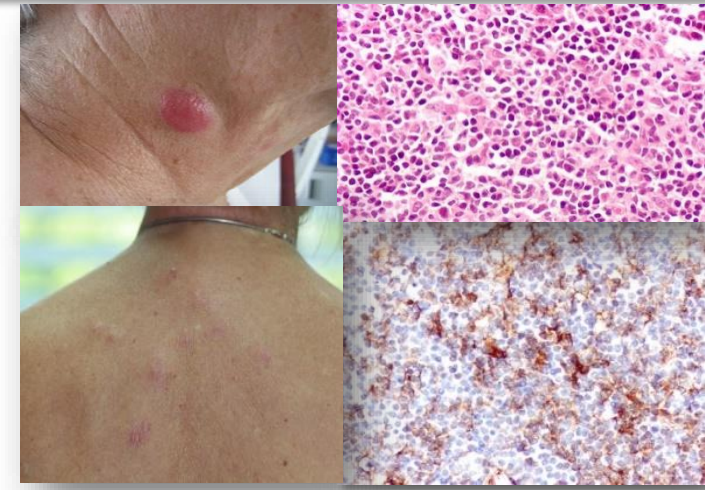


Primary cutaneous large-B cell lymphoma leg-type

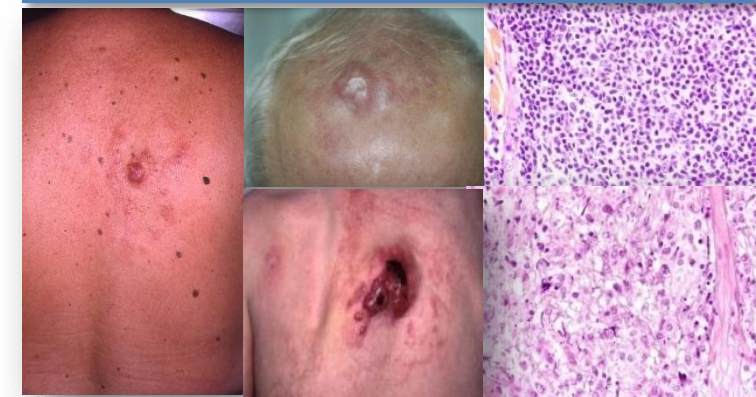


Senff, J Clin Oncol 2007

Primary cutaneous marginal zone lymphoma



Primary cutaneous follicle center lymphoma



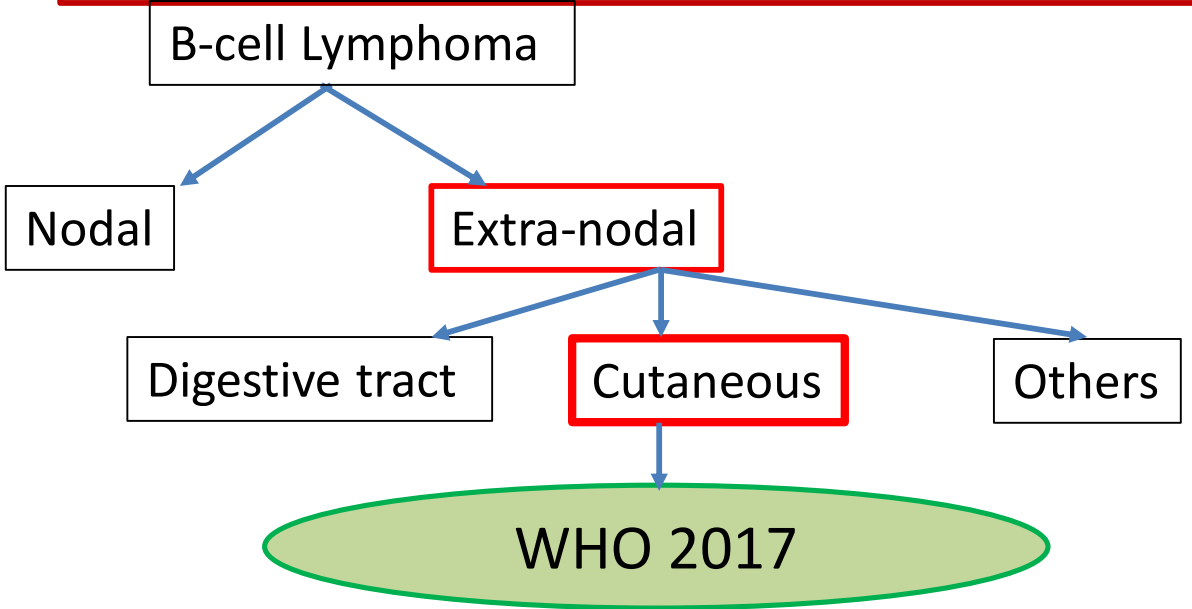
30-50% skin recurrences
 40% extracutaneous spreading : nodes, central nervous system
 5-year survival ≈ 50



Adequate diagnosis is crucial for an adapted treatment



May be challenging for pathologists



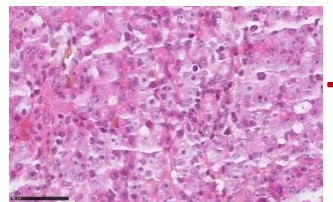
Marginal zone lymphoma

Primary cutaneous follicle centre lymphoma (PCFCL)

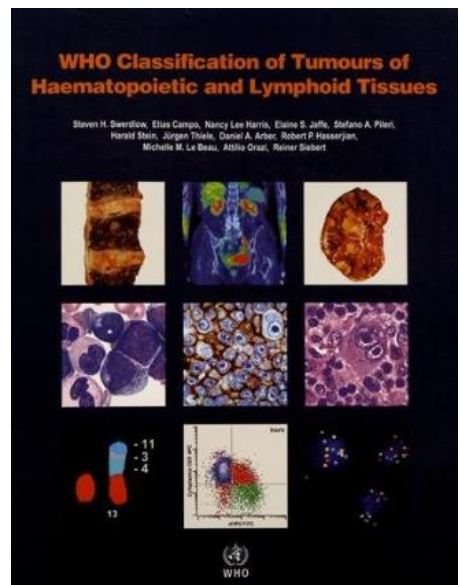
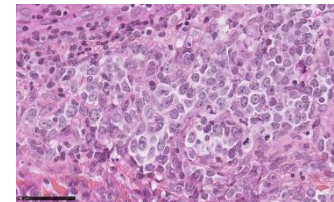
Primary cutaneous diffuse large B-cell lymphoma, leg-type (PCDLBCL-LT)

Small cells

Large cells (PCFCL-LC)



To be distinguished ++



WHO classification of tumours of haematopoietic and lymphoid tissues. Revised 4th edition. (Swerdlow SH, Campo E, Harris NL, et al., eds.). Lyon: International Agency for Research on Cancer; 2017.

Phenotype in PCBCL-large cells: relevant markers for differential diagnosis



Histopathology



2019

Original Article

Primary cutaneous large B-cell lymphomas: relevance of the 2017 World Health Organization classification: clinicopathological and molecular analyses of 64 cases

Sarah Menguy, Marie Beylot-Barry, Marie Parrens, Anne-Pham Ledard, Eric Frison, François Comoz, Maxime Battistella, Vanessa Szablewski, Brigitte Balme, Anne Croue, Frédéric Franck, Nicolas Ortonne, Emilie Tournier, Laurence Lamant, Agnès Carlotti, Anne De Muret, François Le Gall, Marie-Hélène Lorton, Jean-Philippe Merlio, Béatrice Vergier [See fewer authors](#)



Phenotype, n (%)	PCFCL-LC n=25	PCDLBCL-LT n=32	Inclassified n=7
BCL2	7 (28)	32 (100)	6 (86)
MUM1	3 (12)	32 (100)	5 (71)
CD10	14 (56)	0	1 (14)
BCL6	25 (100)	25 (78)	5 (71)
Follicular dendritic meshwork CD21	15 (60)	0	1 (14)
MYC	11 (44)	24 (75)	7 (100)
P63	11 (44)	13 (41)	2 (29)
IgM	2 (8)	14 (44)	2 (29)
FOXP1	2 (8)	25 (78)	4 (57)
Ki67, mean (%) [range]	78 [40–100]	85 [60–100]	83 [60–100]

Adequate staging for an adapted treatment

Clinical evaluation for the skin extension

TNM classification system for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC)

Youn H. Kim,¹ Rein Willemze,² Nicola Pimpinelli,³ Sean Whittaker,⁴ Elise A. Olsen,⁵ Annamari Ranki,⁶ Reinhard Dummer,⁷ and Richard T. Hoppe,⁸ for the ISCL and the EORTC
Blood. 2007;110:479-484

Impact on therapeutic choice and on prognosis

- **T1: solitary lesion**
 - T1a: < 5 cm
 - T1b: > 5 cm
- **T2: Regional skin involvement : 1 anatomic area or 2 contiguous anatomic areas**
 - T2a: all lesions in an area <15 cm
 - T2b: all lesions in an area 15 - 30 cm
 - T2c: all lesions in an area > 30 cm
- **T3: Diffuse skin involvement**
 - T3a: lesions in 2 non-contiguous areas
 - T3b: > 3 anatomic areas





Primary cutaneous lymphoma are, by definition,
« N0, M0 » at diagnosis

- **Clinical examination (T, N?), general status**
- **Blood tests**
 - Blood cell count, liver and kidney analysis
 - **Lactate dehydrogenase**
 - Serum electrophoresis
- **Results of skin biopsy**
- **Molecular analysis in skin biopsy**
 - PCR for IgH rearrangement (value mostly for « staging »)
 - MyD88 mutation





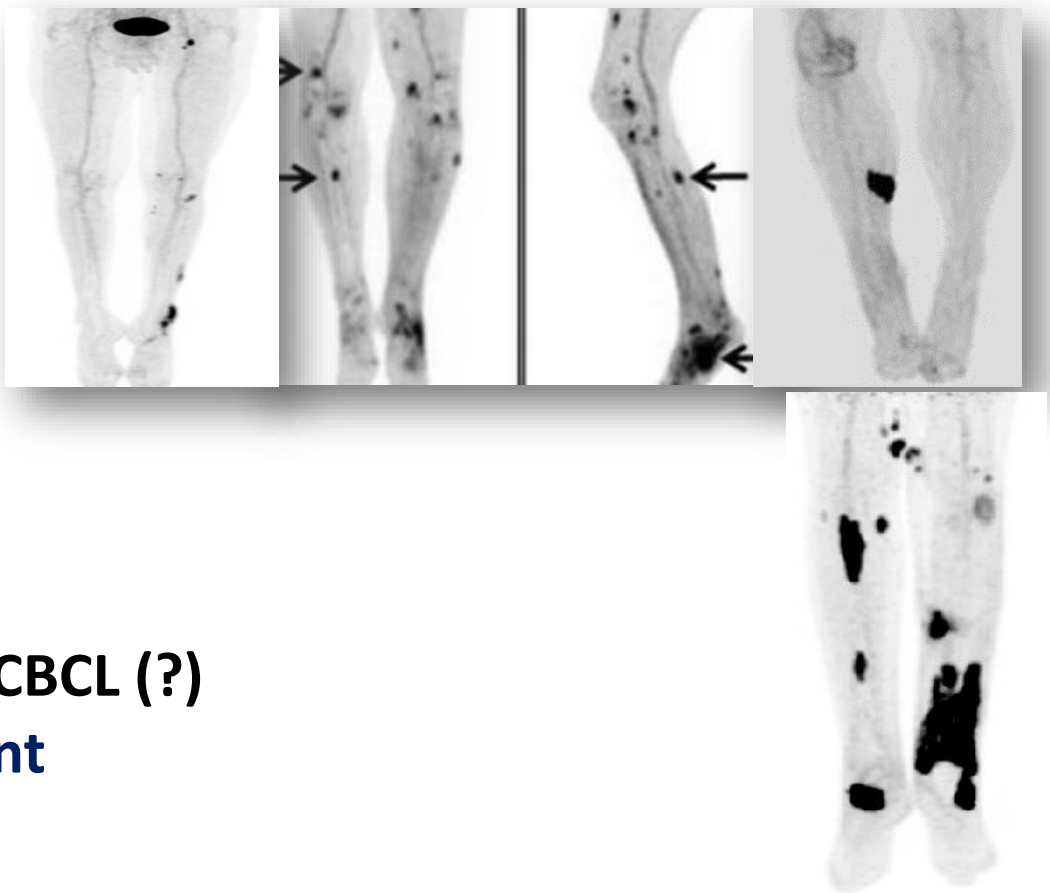
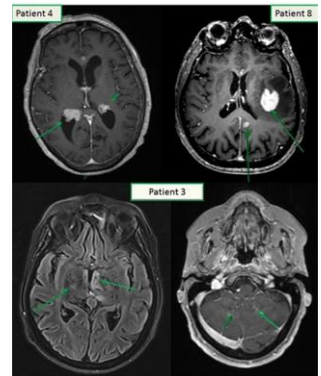
Primary cutaneous lymphoma are, by definition, « N0, M0 » at diagnosis



• Imaging :

- Total body CT-scan
- *Cerebral CT-scan ?*
- *PET scan*

– *Initial staging and monitoring tumor response*



• Bone marrow biopsy

- Recommended for intermediate or aggressive PCBCL (?)
- But debatable for impact on patient management



How to treat these patients ? Limits to therapeutic guidelines

European Organization for Research and Treatment of Cancer and International Society for Cutaneous Lymphoma consensus recommendations for the management of cutaneous B-cell lymphomas

Nancy J. Senff,¹ Evert M. Noordijk,² Youn H. Kim,³ Martine Bagot,⁴ Emilio Berti,⁵ Lorenzo Cerroni,⁶ Reinhard Dummer,⁷ Madeleine Duvic,⁸ Richard T. Hoppe,⁹ Nicola Pimpinelli,¹⁰ Steven T. Rosen,¹¹ Maarten H. Vermeer,¹ Sean Whittaker,¹² and Rein Willemze¹

Blood. 2008;112:1600-1609

- **Guidelines largely based on retrospective studies and institutional experience**
- **No randomized, controlled trials**
- **Large retrospective comparative analysis and one phase 2 study**

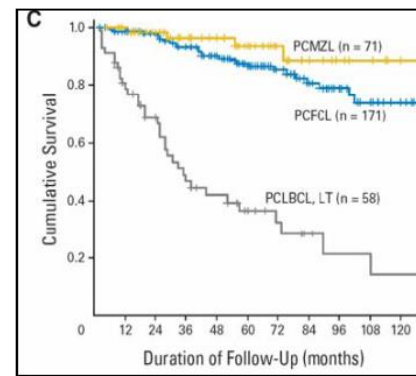


How to treat these patients ? Limits due to the patients



- **Elderly patients...**

Senff 2007



N Engl J Med, Vol. 346, No. 4 · January 24, 2002

CHOP PLUS RITUXIMAB VS. CHOP ALONE IN ELDERLY PATIENTS WITH DIFFUSE LARGE-B-CELL LYMPHOMA

CHOP CHEMOTHERAPY PLUS RITUXIMAB COMPARED WITH CHOP ALONE
IN ELDERLY PATIENTS WITH DIFFUSE LARGE-B-CELL LYMPHOMA

BERTRAND COIFFIER, M.D., ERIC LEPAGE, M.D., PH.D., JOSETTE BRIÈRE, M.D., RAOUL HERBRECHT, M.D., HÉRVÉ TILLY, M.D.,
REDA BOUABDALLAH, M.D., PIERRE MOREL, M.D., ERIC VAN DEN NESTE, M.D., GILLES SALLES, M.D., PH.D.,
PHILIPPE GAULARD, M.D., FELIX REYES, M.D., AND CHRISTIAN GISSELBRECHT, M.D.

30-50% skin recurrences
40% extracutaneous spreading : nodes, central nervous system
5-year survival ≈ 50

Feugier et al. J Clin Oncol 2005



What about PCDLBC-LT ?



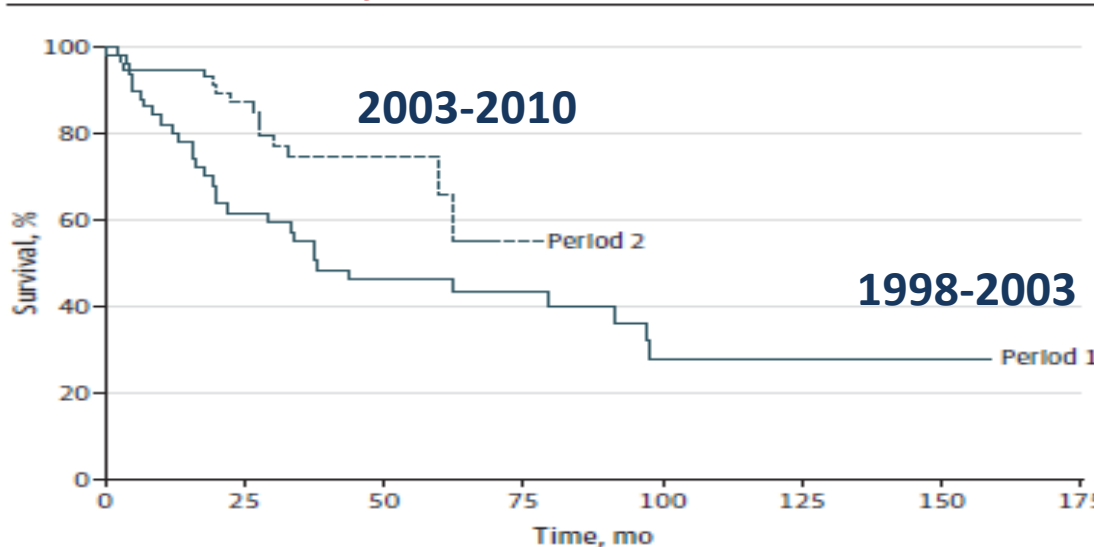
Improvement of Survival in Patients with Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type, in France

Florent Grange, MD, PhD; Pascal Joly, MD, PhD; Coralie Barbe, MD; Martine Bagot, MD, PhD; Stéphane Dalle, MD, PhD; Saskia Ingen-Housz-Oro, MD; Eve Maubec, MD, PhD; Michel D'Incan, MD, PhD; Caroline Ram-Wolff, MD; Sophie Dalac, MD; Isabelle Templier, MD; Eric Esteve, MD; Gaëlle Quereux, MD, PhD; Laurent Machet, MD, PhD; Marion Leduc, MSc; Olivier Dereure, MD, PhD; Liliane Laroche, MD, PhD; Philippe Saiag, MD, PhD; Béatrice Vergier, MD, PhD; Marie Beylot-Barry, MD, PhD



Specific survival of 115 French patients with PCLBCL, LT, according to period of diagnosis : improvement of survival between the two periods

5-y survival : 66% vs 46% P = 0,01

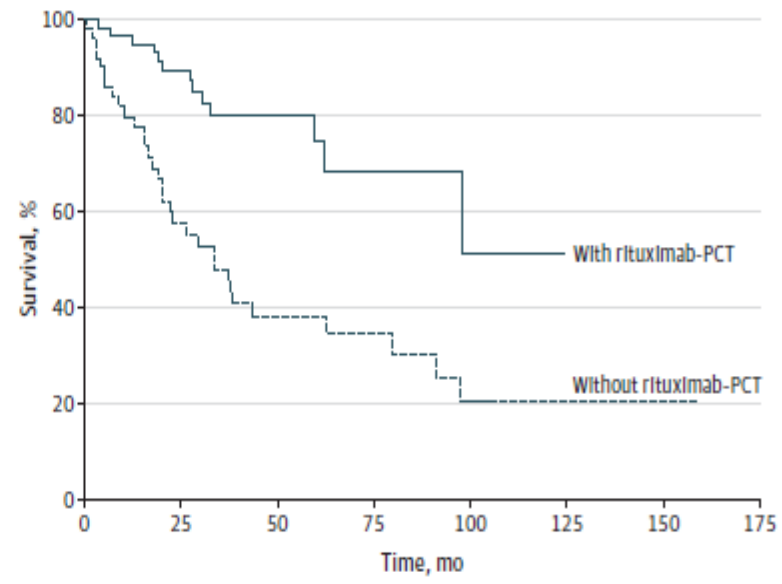
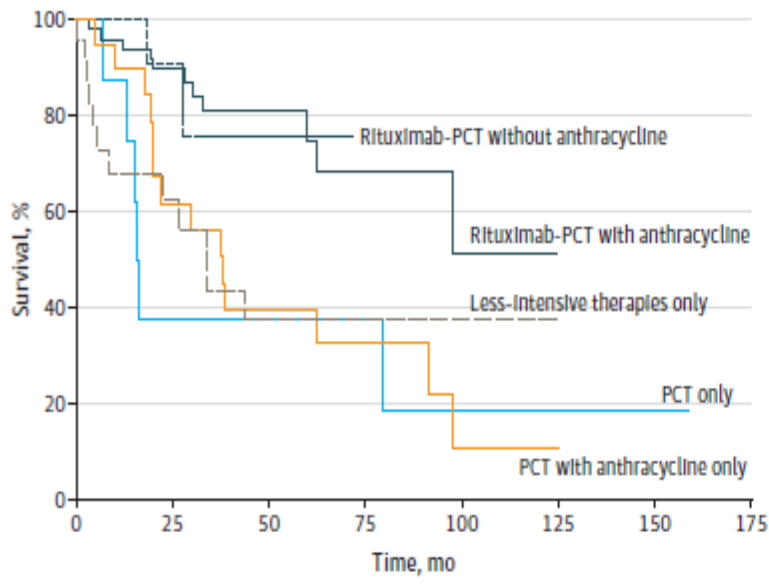


	Period 1 (1998-2003)	Period 2 (2004-2010)	p
N = 115	54	61	
gender (%F)	61%	57%	0,68
Age	76	78	0,37
T1	33%	22%	0,16
Leg location	72.2%	85.2%	0,09
Radiotherapy	44%	16%	<0,0001
R-C(H)OP*	17%	88%	<0,0001





Improvement of survival is associated with R-C(H)OP regimens in patients with PCLBCL-LT



Characteristic	Patients Receiving Rituximab-PCT (n = 63)	Patients Receiving Other Treatment (n = 52) ^a	<i>P</i> Value ^b
Complete response	55 (87.3)	32 (61.5)	.001
Specific survival rate, %			
3 y	80	48	<.001
5 y	74	38	

Characteristic	HR (95% CI)	<i>P</i> Value
No. of skin lesions		
1	1 [Reference]	.07
>1	2.0 (0.9-4.2)	
Type of treatment		
Without rituximab-PCT	1 [Reference]	<.001
With rituximab-PCT	4.6 (2.4-9.1)	
Location		
Nonleg	1 [Reference]	.06
Leg	2.4 (1.0-6.1)	

74% 5-year specific survival

Overcomes negative effects of typical adverse prognostic factors (leg location, extent of skin lesions)



R-C(H)OP to be considered in first line in large B-cell lymphoma leg-type as it has been demonstrated to improve survival



• Advanced-age patients :

- Age adapted regimens
- R-CHOP, R-miniCHOP, R-COP +/- radiotherapy (?)
- *Alternative associations* : R + pegylated liposomal doxorubicine (less cardiotoxicity++)
- NB : Rituximab monotherapy : short-term responses++

Grange F. Arch Dermatol 2009
Guyot A., Arch Dermatol 2010

Fabbry A. Eur J Haematol 2014

SUPPORTIVE CARE ++ (gastric protection / high dose corticosteroids; haematopoietic growth factors, infectious prevention (lymphopenia, hypogammaglobulinemia))



Radiotherapy in PCLBCL-LT ?



In localized disease, without
Rituximab and chemo

→ Palliative effect

→ Relapses++

- **Associated to the rituximab-chemo?**

- no trial

**National Comprehensive Cancer Network.
NCCN guidelines 2018 & Gilson D. et al. Br J
Dermatol 2019.*

- in recent guidelines*

- For all patients after R-chemo ?

- In refractory cases ? (Partial response after
systemic R-chemo)

- Recurrences may be seen on treated and untreated
areas

Christensen L. et al. Br J Dermatol 2018



Even with R-Chemo : 40% recurrences

Therapeutic choice in case of recurrence or progression
➔ **Further complicated in already treated, advanced-age patients, co-morbidities?**

↗ **New therapeutic options and strategies**

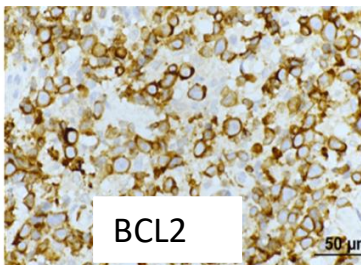
↘ **Predictive markers for response or recurrence ?**



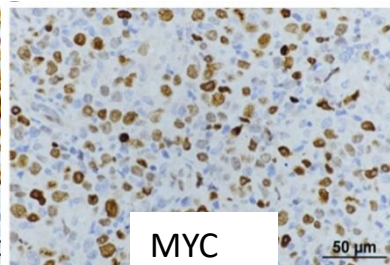
Modern Pathology (2018) 31:1332–1342

Double-hit or dual expression of MYC and BCL2 in primary cutaneous large B-cell lymphomas

Sarah Menguy^{1,2} · Eric Frison³ · Martina Prochazkova-Carlotti¹ · Stephane Dalle⁴ · Olivier Dereure⁵ · Serge Boulinguez⁶ · Sophie Dalac⁷ · Laurent Machet⁸ · Caroline Ram-Wolff⁹ · Laurence Verneuil¹⁰ · Audrey Gros^{1,11} · Béatrice Vergier^{1,2} · Marie Beylot-Barry^{1,12} · Jean-Philippe Merlio^{1,11} · Anne Pham-Ledard^{1,12}



BCL2



MYC

Journal of Investigative Dermatology (2019) 139, 2334–2342; doi:10.1016/j.jid.2019.05.011

ORIGINAL ARTICLE

Mutations of the B-Cell Receptor Pathway Confer Chemoresistance in Primary Cutaneous Diffuse Large B-Cell Lymphoma Leg Type

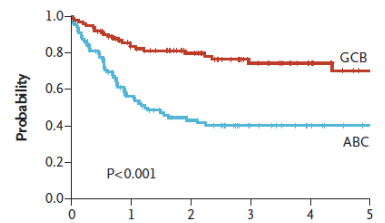
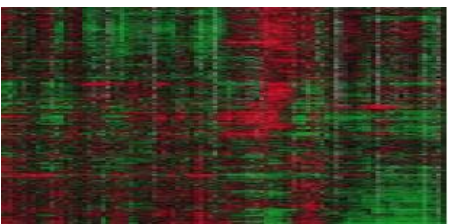
Océane Ducharme^{1,2}, Marie Beylot-Barry^{1,2}, Anne Pham-Ledard^{1,2}, Elodie Bohers³, Pierre-Julien Vially³, Thomas Bandres⁴, Nicolas Faur³, Eric Frison⁵, Béatrice Vergier^{2,6}, Fabrice Jardin³, Jean-Philippe Merlio^{2,4} and Audrey Gros^{2,4}





Diffuse large B-cell lymphomas: Gene expression profiling => Two main subtypes

« GC » vs « ABC or post GC »

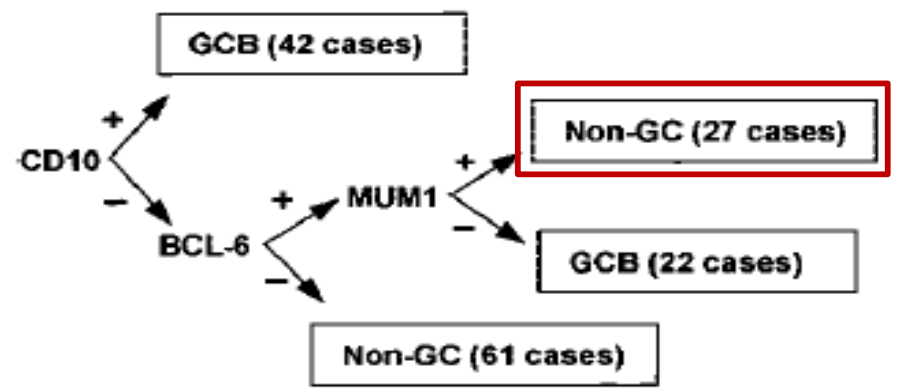


→ Activated B-cell :

- Worse prognosis
- Constitutive NF-kB activation
- Distinct oncogenic pathways

Phenotype:

→ Hans Algorithm



Primary cutaneous B-cell lymphoma Leg-type
 CD10-, BCL6+, MUM1/IRF4+, BCL2+
 → « ABC » type profile

Djikman J Clin Oncol 2006
 Hoefnagel, Blood, 2005
 Menguy, Histopathology 2019

Alizadeh, Nature, 2000 Hans, Blood, 2004
 Lenz, PNAS 2008 Lenz N Engl J Med 2010

Advances in biological knowledge



Journal of Investigative Dermatology (2012), Volume 132

MYD88 Somatic Mutation Is a Genetic Feature of Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type

Anne Pham-Ledard^{1,2,5},
David Cappellen^{1,3,5},
Fabian Martinez³, Béatrice Vergier⁴,
Marie Beylot-Barry^{1,2} and
Jean-Philippe Merlio^{1,3}



Journal of Investigative Dermatology (2016),

MYD88 Somatic Mutation Is a Diagnostic Criterion in Primary Cutaneous Large B-Cell Lymphoma

Sarah Menguy^{1,2,17}, Audrey Gros^{1,3,17},
Anne Pham-Ledard^{1,4},
Maxime Battistella⁵, Nicolas Ortonne⁶,
François Comoz⁷, Brigitte Balme⁸,
Vanessa Szablewski⁹,
Laurence Lamant¹⁰, Agnès Carlotti¹¹,
Marie-Hélène Lorton¹², Anne de Muret¹³, François Le Gall¹⁴,
Frédéric Franck¹⁵, Anne Croue¹⁶,
David Cappellen^{1,3},
Marie Beylot-Barry^{1,4},
Jean-Philippe Merlio^{1,3,*} and
Béatrice Vergier^{1,2}

Journal of Investigative Dermatology (2017)

Identification of Somatic Mutations in Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type by Massive Parallel Sequencing

Sylvain Mareschal¹, Anne Pham-Ledard^{2,3}, Pierre Julien Viailly¹, Sydney Dubois¹, Philippe Bertrand¹, Catherine Maingonnat¹, Maxime Fontanilles¹, Elodie Bohers¹, Philippe Ruminy¹, Isabelle Tournier⁴, Philippe Courville⁵, Bernard Lenormand⁵, Anne Bénédicte Duval⁵, Emilie Andrieu⁵, Laurence Verneuil⁶, Beatrice Vergier^{2,3}, Hervé Tilly¹, Pascal Joly⁴, Thierry Frebourg⁴, Marie Beylot-Barry^{2,3}, Jean-Philippe Merlio^{2,3} and Fabrice Jardin¹



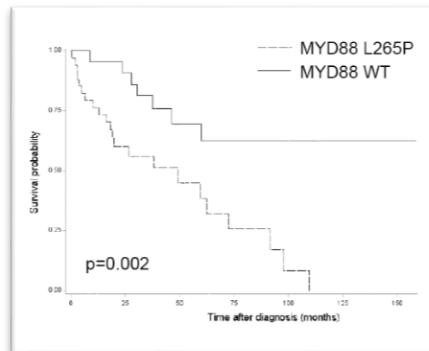
JAMA Dermatol 2014

Original Investigation

Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg-Type High Frequency and Clinical Prognostic Value of MYD88 L265P Mutation

Anne Pham-Ledard, MD; Marie Beylot-Barry, MD, PhD; Coralie Barbe, MD; Marion Leduc, MS; Tony Petrella, MD; Béatrice Vergier, MD, PhD; Fabian Martinez, MS; David Cappellen, PhD; Jean-Philippe Merlio, MD, PhD; Florent Grange, MD, PhD

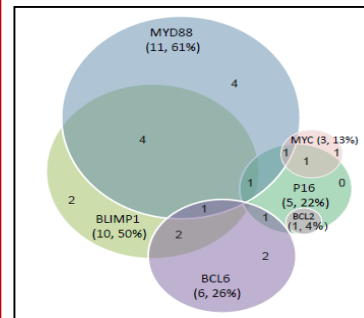
Overall survival according to MYD88 status



MODERN PATHOLOGY (2013), 1–10

Multiple genetic alterations in primary cutaneous large B-cell lymphoma, leg type support a common lymphomagenesis with activated B-cell-like diffuse large B-cell lymphoma

Anne Pham-Ledard^{1,2}, Martina Prochazkova-Carlotti¹, Laetitia Andrique¹, David Cappellen^{1,3}, Béatrice Vergier⁴, Fabian Martinez³, Florent Grange⁵, Tony Petrella⁶, Marie Beylot-Barry^{1,2} and Jean-Philippe Merlio^{1,3}



WES/NGS ciblé :

Combinaison de mutations MYD88, PIM1 CD79B, IRF4, délétions CDKN2A/2B, BLIMP1



Journal of Investigative Dermatology (2018),

Genomic Analyses Identify Recurrent Alterations in Immune Evasion Genes in Diffuse Large B-Cell Lymphoma, Leg Type

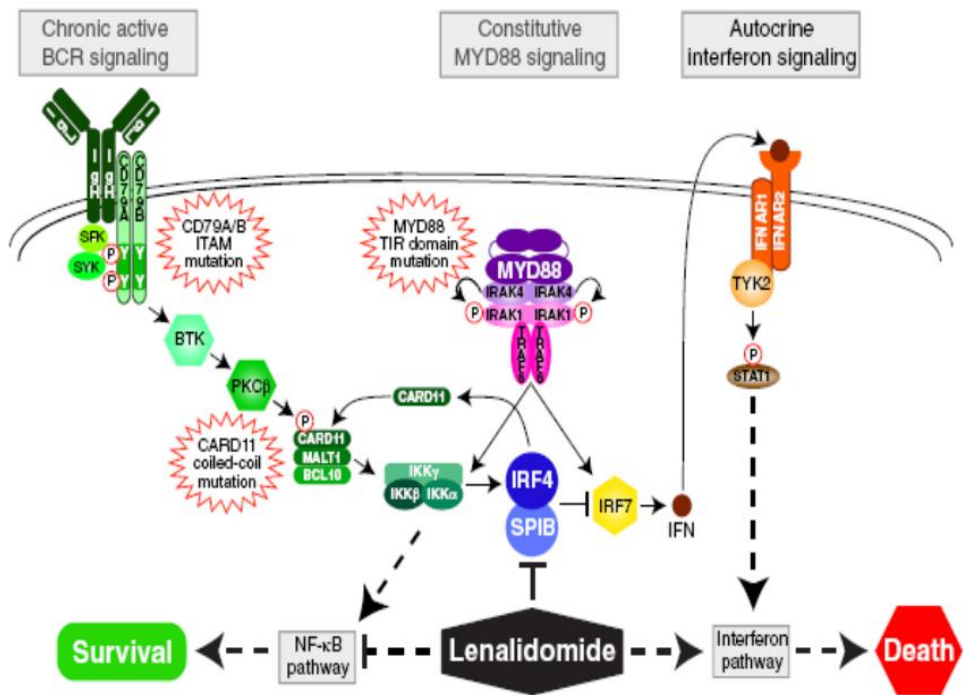
Xiaolong Alan Zhou^{1,12}, Abner Louissaint Jr.^{2,3,12}, Alexander Wenzel⁴, Jingyi Yang^{4,5}, Maria Estela Martinez-Escalá¹, Andrea P. Moy^{2,3}, Elizabeth A. Morgan⁶, Christian N. Paxton⁷, Bo Hong Erica F. Andersen⁸, Joan Guitart¹, Amir Behdad⁹, Lorenzo Cerroni¹⁰, David M. Weinstock^{3,11} and Jaehyuk Choi^{1,4,5}

MYD88 mutation 67-70% : diagnostic and prognostic value

Constitutional activation NF-κB pathway



Exploiting Synthetic Lethality for the Therapy of ABC Diffuse Large B Cell Lymphoma



Lenalidomide as a candidate ?

VOLUME 26 · NUMBER 30 · OCTOBER 20 2008

JOURNAL OF CLINICAL ONCOLOGY

Lenalidomide Monotherapy in Relapsed or Refractory Aggressive Non-Hodgkin's Lymphoma

Peter H. Wiernik, Izidore S. Lossos, Joseph M. Tuscano, Glen Justice, Julie M. Vose, Craig E. Cole, Wendy Lam, Kyle McBride, Kenton Wride, Dennis Pietronigro, Kenichi Takeshita, Annette Ervin-Haynes, Jerome B. Zeldis, and Thomas M. Habermann

Annals of Oncology 22: 1622–1627, 2011

An international phase II trial of single-agent lenalidomide for relapsed or refractory aggressive B-cell non-Hodgkin's lymphoma

T. E. Witzig^{1*}, J. M. Vose², P. L. Zinzani³, C. B. Reeder⁴, R. Buckstein⁵, J. A. Polikoff⁶, R. Bouabdallah⁷, C. Haioun⁸, H. Tilly⁹, P. Guo¹⁰, D. Pietronigro¹⁰, A. L. Ervin-Haynes¹⁰ & M. S. Czuczman¹¹

Yang Cancer Cell 2012

Lenalidomide monotherapy in relapsed primary cutaneous diffuse large B cell lymphoma-leg type

P. Savini · A. Lanzi · F. G. Foschi · G. Marano · G. F. Stefanini

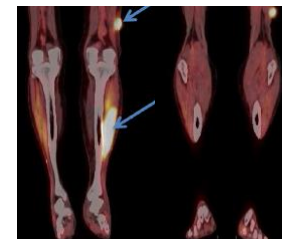
Ann Hematol (2014) 93:333–334



Remission induction with lenalidomide in a patient with relapsed diffuse large B cell lymphoma of the leg type

Abhisek Swaika · David M. Menke · Manoj K. Jain · Taimur Sher

Ann Hematol (2015) 94:895–896





A Single-Arm Phase II Trial of Lenalidomide in Relapsing or Refractory Primary Cutaneous Large B-Cell Lymphoma, Leg Type



Marie Beylot-Barry^{1,2,19}, Diane Mermin^{1,19}, Aline Maillard³, Reda Bouabdallah⁴, Nathalie Bonnet⁵, Anne-Bénédicte Duval-Modeste⁶, Laurent Mortier⁷, Saskia Ingen-Housz-Oro⁸, Caroline Ram-Wolf⁹, Stéphane Barete¹⁰, Stéphane Dalle¹¹, Eve Maubec^{12,20}, Gaëlle Quereux¹³, Isabelle Templier¹⁴, Martine Bagot⁹, Florent Grange¹⁵, Pascal Joly⁶, Béatrice Vergier^{2,16}, Pierre-Julien Vially¹⁷, Audrey Gros^{2,18}, Anne Pham-Ledard^{1,2}, Eric Frison³ and Jean-Philippe Merlio^{2,18}



Lenalidomide : 25 mg daily for 21/28 day-cycle

Treatment maintained 12 months unless progression

Primary endpoint : overall response (OR = CR + PR) at 6 months.

19 patients, med age 79 ans (69-92), 18/19 : leg location, 16/19 : Relapse after CR; Stages: T1 (n=2), T2 (n=13), T3 (n=4)

Median nbr of cycles = 5

63% ORR

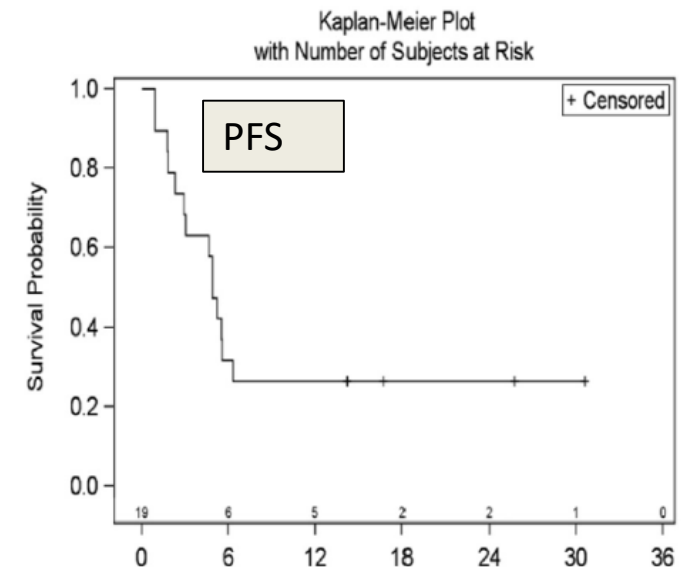
but RR at 6 months = 26.3% (11%-47.6%, 90%CI) including 4 CR and 1 PR)

At 12 months, 3 still treated : 2 CR and 1 PR.

Median PFS = 5 months (1-31)

Overall survival 6 and 12 months : 89.5% and 68.4%

Median overall survival 19 months



Survival probabilities (95%CI)

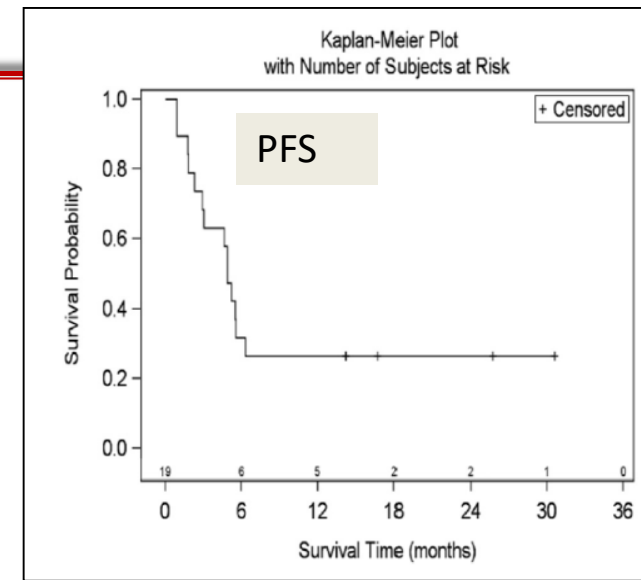
	Overall survival	Specific survival
6 months	89.5% (64.1-97.3)	100%
12 months	68.4% (42.8-84.4)	76.5 % (48.9-90.4)
24 months	36.3% (12.7-60.7)	40.5 % (14.0-66.0)



A Single-Arm Phase II Trial of Lenalidomide in Relapsing or Refractory Primary Cutaneous Large B-Cell Lymphoma, Leg Type



Marie Beylot-Barry^{1,2,19}, Diane Mermin^{1,19}, Aline Maillard³, Reda Bouabdallah⁴, Nathalie Bonnet⁵, Anne-Bénédicte Duval-Modeste⁶, Laurent Mortier⁷, Saskia Ingen-Housz-Oro⁸, Caroline Ram-Wolff⁹, Stéphane Barete¹⁰, Stéphane Dalle¹¹, Eve Maubec^{12,20}, Gaelle Quereux¹³, Isabelle Templier¹⁴, Martine Bagot⁹, Florent Grange¹⁵, Pascal Joly⁶, Béatrice Vergier^{2,16}, Pierre-Julien Vially¹⁷, Audrey Gros^{2,18}, Anne Pham-Ledard^{1,2}, Eric Frison³ and Jean-Philippe Merlio^{2,18}



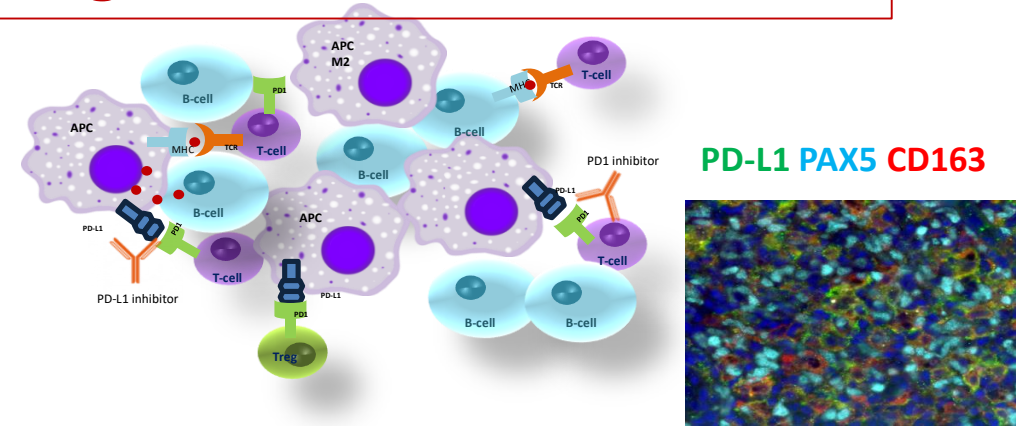
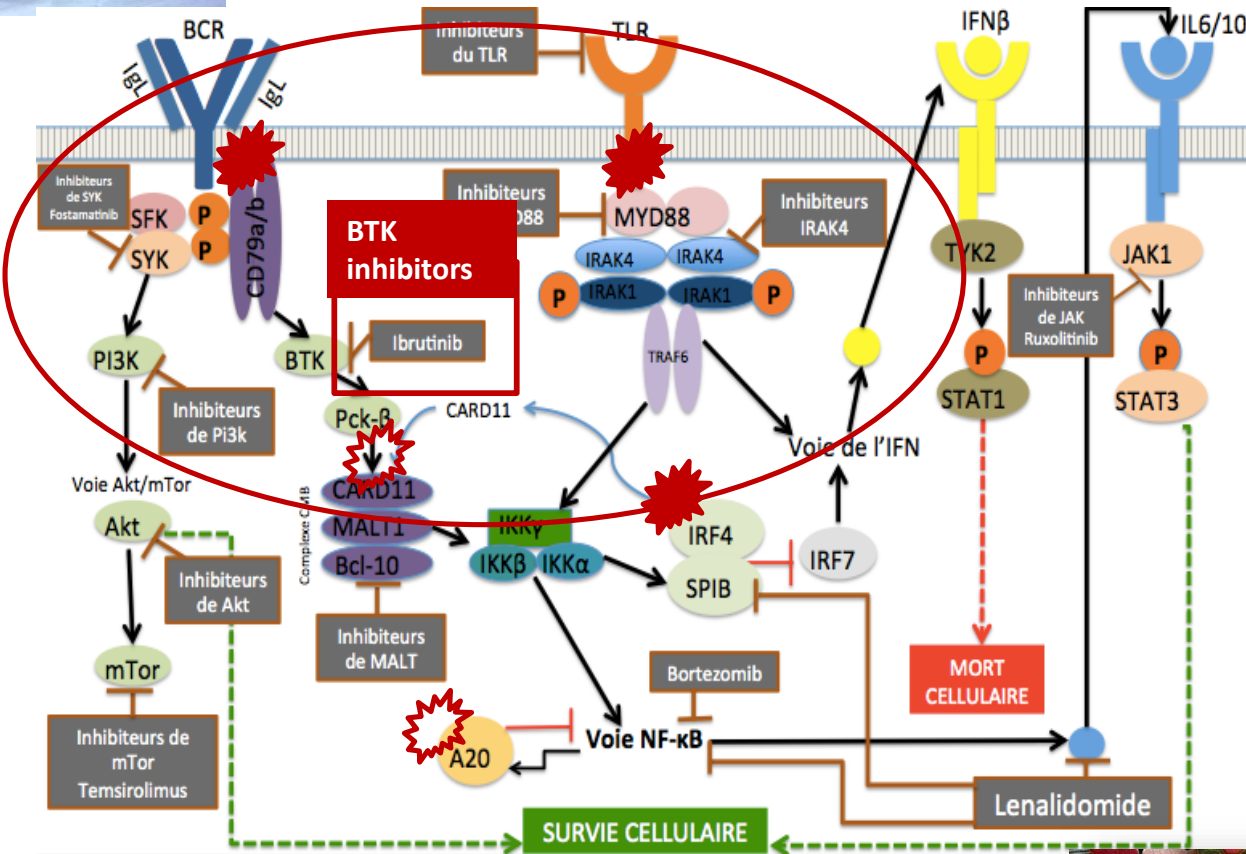
- **Severe AEs (11 grade 3 in 7 patients and 2 deaths) and dose reduction due to Aes in 7 patients (cytopenia, thromboembolic)**
- **However, a prolonged response (including CR) was obtained in some patients :**
 - 60% of patients who achieved response at M6 had a durable response and were still responders at 12 months
 - Patients treated in the second year of the trial vs first year
 - **Dose reduced** for AEs : 62.5% vs 36.4%
 - **Higher number of cycles** : median = 7 (5-12) vs 4 (1-5)
 - **Better survival** deaths = 25% vs 81.8%

- **Reduced dosage in such patients ?**
- **Association with Rituximab ?**
- **Maintenance therapy after R-CHOP in high risk patients ?** *Thieblemont C. et al. J Clin Oncol 2017*
- **Personalized medicine with NGS profile?**



Cooperation / different pathways

Target microenvironnement



Cooperation between pathways → Synergistic combined therapies ?



AmJ Surg Pathol. 2017

Tumor Microenvironment and Checkpoint Molecules in Primary Cutaneous Diffuse Large B-Cell Lymphoma—New Therapeutic Targets

Christina Mitteldorf, MD,* Arbeneshe Berisha, BSc,† Monique C. Pfaltz, PhD,‡
Sigrid M.C. Broekaert, MD,§ Michael P. Schön, MD,§ Katrin Kerl, MD,¶
and Werner Kempf, MD,‡*

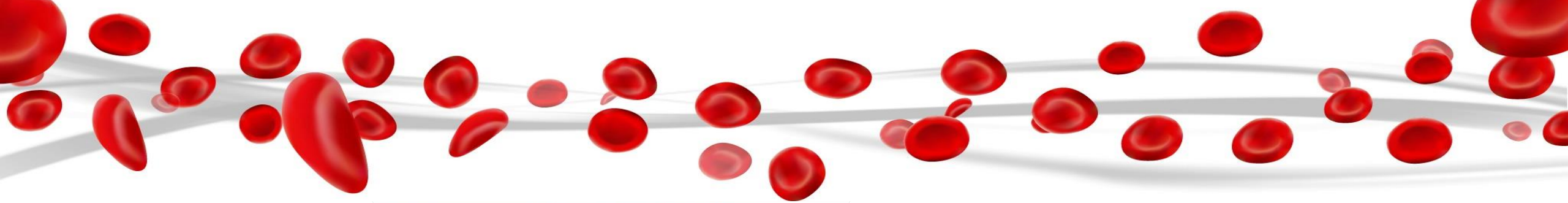
PD-L1 and PD-L2 Are Differentially Expressed by Macrophages or Tumor Cells in Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type

Sarah Menguy, MD,*† Martina Prochazkova-Carlotti, PhD,* Marie Beylot-Barry, MD, PhD,*‡
Frédéric Saltel, PhD,§ Béatrice Vergier, MD, PhD,*†
Jean-Philippe Merlio, MD, PhD,*|| and Anne Pham-Ledard, MD, PhD,*‡

Journal of Investigative Dermatology (2018),

Genomic Analyses Identify Recurrent Alterations in Immune Evasion Genes in Diffuse Large B-Cell Lymphoma, Leg Type

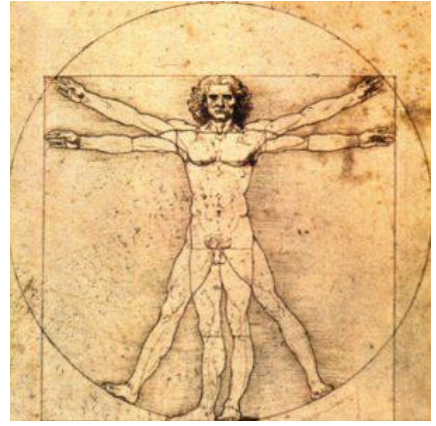
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Jaehyuk Choi^{1,4,5}



INSERM U1053 UMR BaRITON; Team 3 : Oncogenesis of cutaneous lymphoma

University of Bordeaux

- Jean Philippe Merlio**
- Marie Beylot-Barry**
- Béatrice Vergier**
- Anne Pham-Ledard**
- Edith Chevret**
- Sandrine Poglio**
- Audrey Gros**
- Laurence Bresson-Bepoldin**
- Martina Carlotti**
- Sarah Menguy**
- Élodie Laharanne**
- Yamina Idrissi**
- Alexandra Prévot**
- Alban Giese**
- Lamia Azzi-Martin**
- Jacky Ferrer**



Accueil Aide

Se connecter | Mot de passe oublié

Actualité

- 1) Accueil
- 2) Actualités
- 3) Autres événements

Objectifs & Fonctionnement

- 1) Objectifs
- 2) Fonctionnement
- 3) Charte d'utilisation
- 4) Statuts du GFELC

Recommandations

- 1) Recommandations
- 2) Protocoles
- 3) Enseignement
- 4) Bibliographie GFELC
- 5) Information du Patient

Contact & Support

- 1) Contact & Support

Le GFELC rassemble 31 équipes pluridisciplinaires (les « Centres ») constituées, chacune, d'un dermatologue et d'un pathologiste et, pour certaines, d'un biologiste moléculaire. Il constitue, officiellement, un Centre de Référence National pour les Lymphomes Cutanés, chaque centre étant considéré comme un Centre de Compétence. Il est constitué en Association de type Loi 1901. Le GFELC est un groupe thématique de recherche de la Société Française de Dermatologie.



Webinars
Cutaneous Lymphoma