Conduite à tenir devant une hyperlymphocytose

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Définition

- Présence d'un taux excessif de lymphocytes sur l'hémogramme
  - > 4500/mm3 chez un adulte
  - > 8000/mm3 chez un enfant (lymphocytose physiologique jusqu'à 2 ans et dans moindre mesure jusqu'à 8-10 ans)

Problèmes techniques

- confusion avec un syndrome mononucléosique
- confusion avec des cellules lymphoïdes atypiques (p.ex. tricholeucocytes)
- confusion petits blastes de leucémie aiguë lymphoblastique

conséquences ?

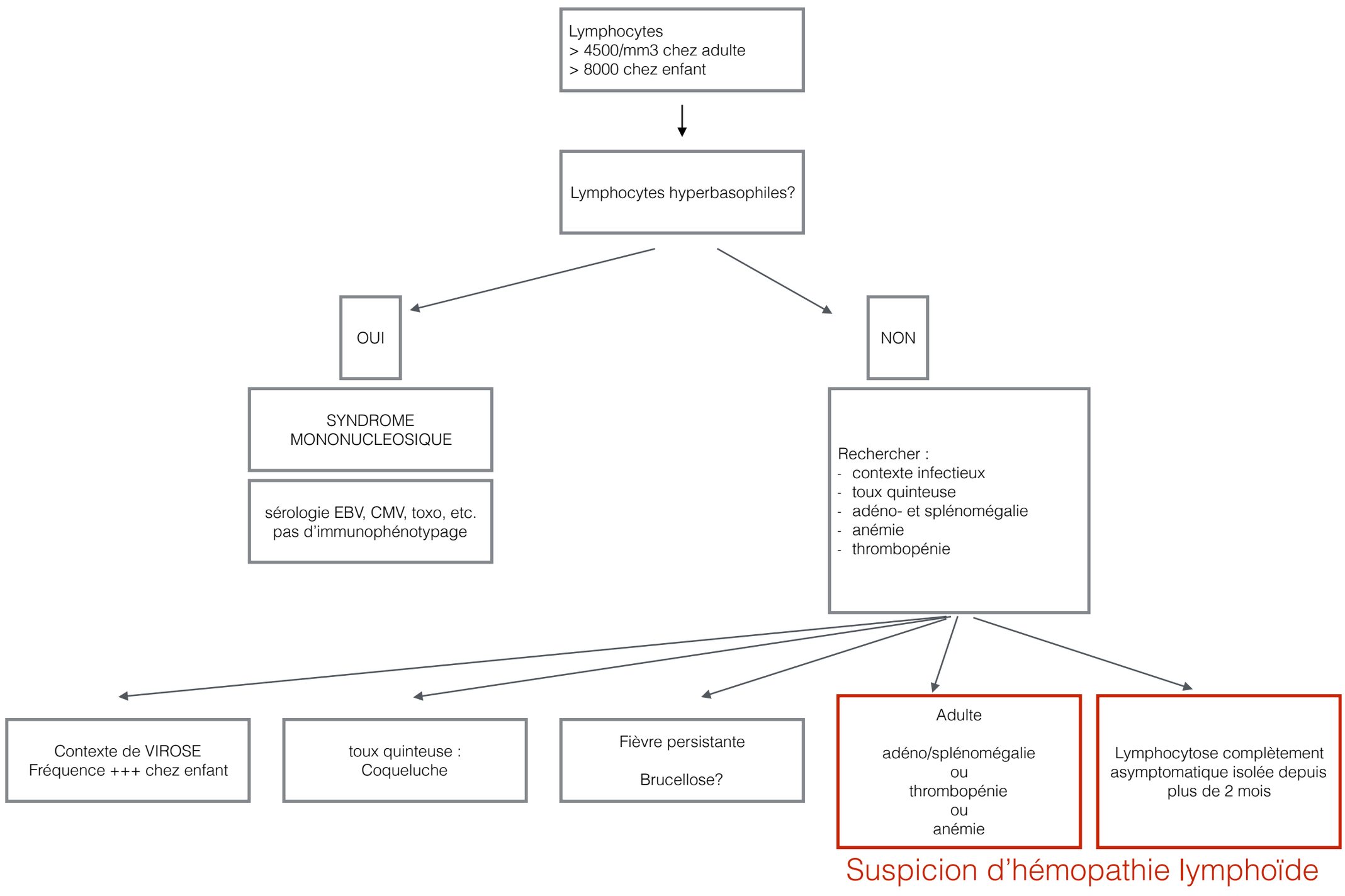
- les hyperlymphocytoses même importantes n'ont habituellement pas de conséquence

- la viscosité sanguine n'est augmentée que pour des chiffres > 500 000/mm3

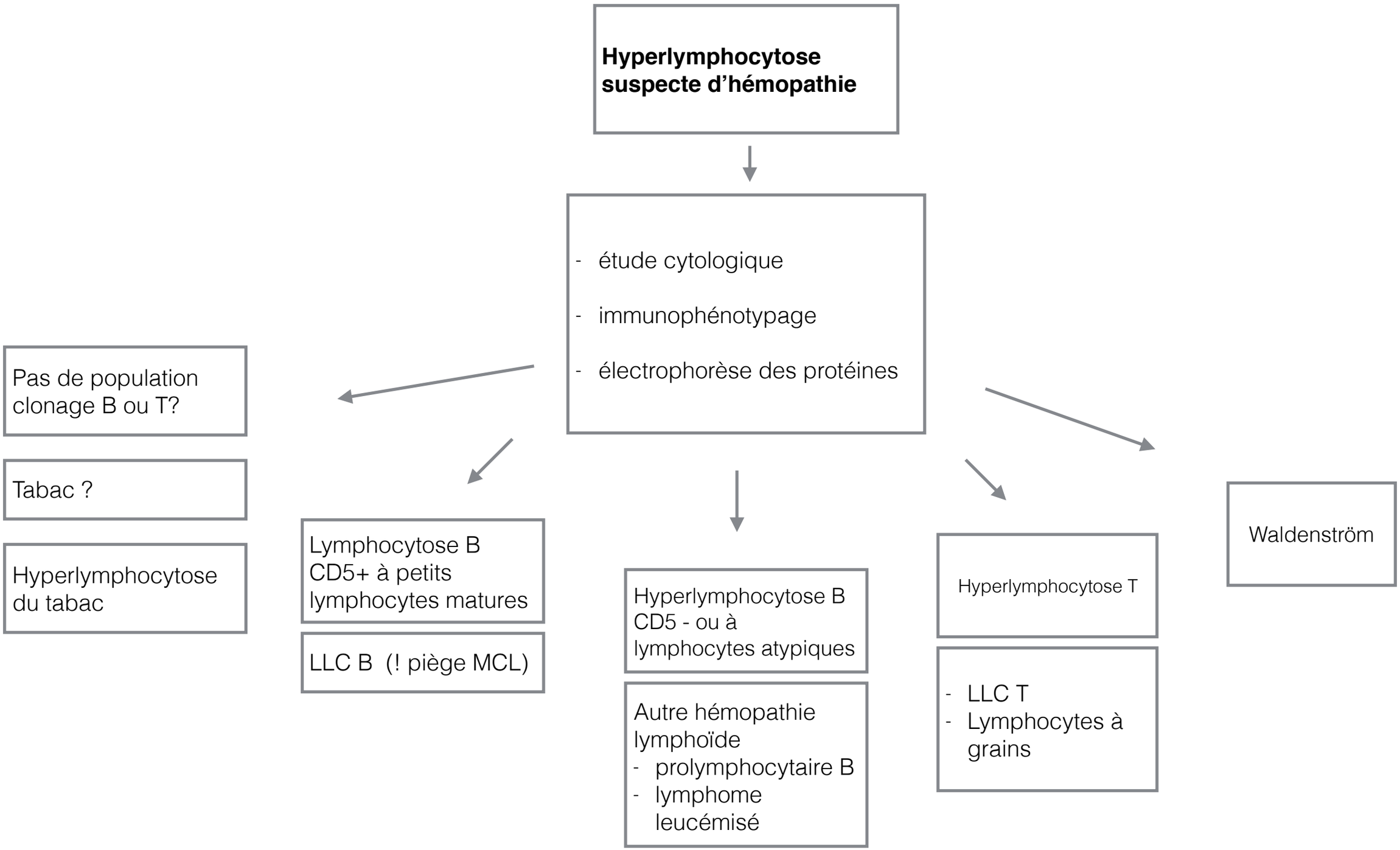
Diagnostic etiologique

- Réactionnelle
    - Pathologie infectieuse (cause n°1 chez l'enfant)
        - Coqueluche (lymphocytose élevée 15-30 Giga/L parfois 100!) et Maladie de Carl-Smith (pratiquement asymptomatique en dehors d'un éventuel syndrome fébrile et de rash cutané, rarement > 50 Giga/L)
        - Adénoviroses et viroses non spécifiques
        - Plus rarement : brucellose, thyreotoxicose, syphilis, tuberculose, rickettsioses, endocardite bactérienne
- Hémopathie lymphoïde

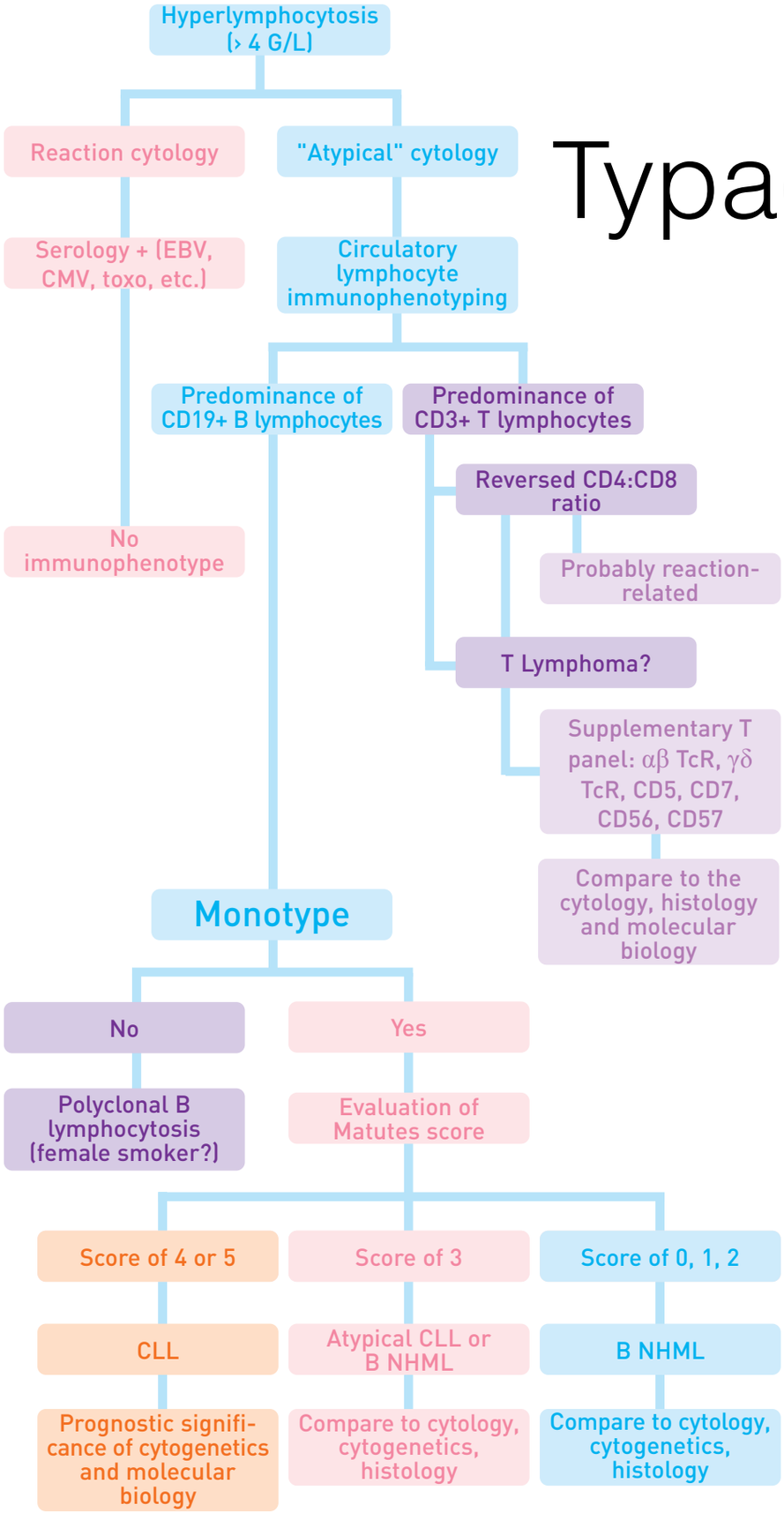
Diagnostic etiologique



Diagnostic étiologique



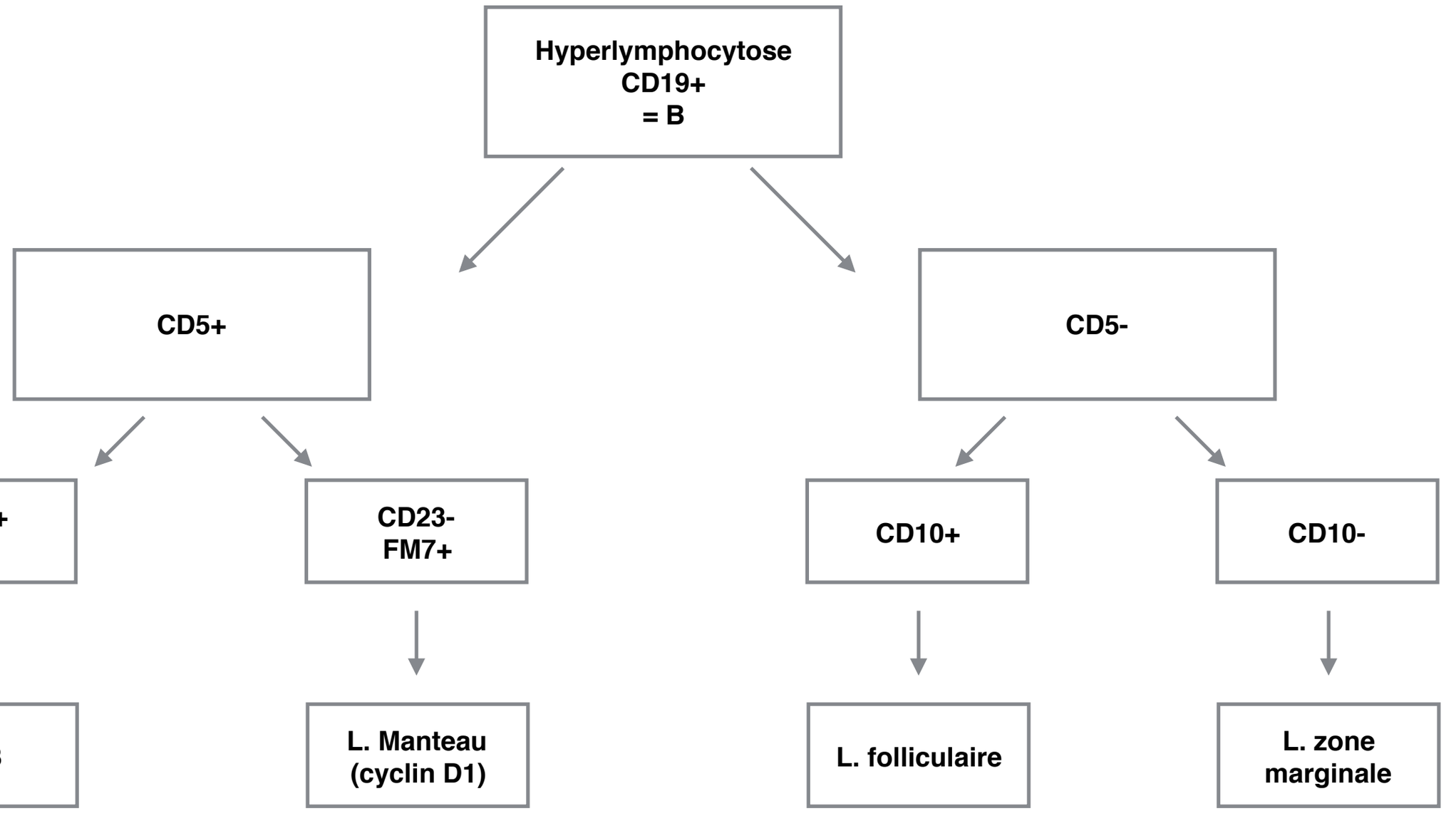
Typage lymphocytaire



	CLL	Tricho	FL	MCL	MZL
Kappa Lambda	+	+/++	+++	++	+/++
CD19	++	+	+	+	+
CD10	-	-/+	+/++	-	-
CD20	+ low	+++	+	+	+
CD22	-	++	+	+	+++/+
CD23	++	-	+	-	-/+
FMC7	-	+++	+/-	++	++/-
CD5	++	+/-	-	++	-
CD11c	+ low	+	-	-	+/-
CD25	+ low	++	-	-	+/-
CD103	-	+++	-	-	-
CD43	++	-	-	+++/+	+/-
CD79b	+/-	-	++	++	+
CD38	-/+	-/+	-/+	-/+	-
CD43	+		-	+	

CLL: Chromic lymphocytic leukaemia; **FL:** Follicular lymphoma; **MCL:** Mantle Cell Lymphoma; **MZL:** Marginal zone lymphoma; **Tricho:** Tricholeukocytic leukaemia

Typage lymphocytaire



Score de Matutes

Membrane markers	Points	
	1	0
Surface immunoglobulin (Kappa or Lambda) expression	Low	Moderate or high
CD5	+	-
CD22	-/low	Moderate/High
CD23	+	-
FMC7	-	+

Interpretation of score:

- Score of 5/5 and 4/5: CLL.
- Score of 3/5: atypical CLL or B lymphoma.
- Scores of 0/5, 1/5 and 2/5: not CLL, but B lymphoma.

Existent des variantes, certains remplacent CD22 par CD79b, d'autres utilisent un score à 6 points incluant CD79b

Matutes E, *et all*. Leukemia. 1994 Oct;8(10):1640-5.

Classification WHO 2016

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**
- Burkitt lymphoma
- *Burkitt-like lymphoma with 11q aberration**
- High-grade B-cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements*
- High-grade B-cell lymphoma, NOS*
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

Mature T and NK neoplasms

- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- *Chronic lymphoproliferative disorder of NK cells*
- Aggressive NK-cell leukemia
- Systemic EBV^+ T-cell lymphoma of childhood*
- Hydroa vacciniforme–like lymphoproliferative disorder*
- Adult T-cell leukemia/lymphoma
- Extranodal NK-/T-cell lymphoma, nasal type
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma*
- *Indolent T-cell lymphoproliferative disorder of the GI tract**
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous $CD30^+$ T-cell lymphoproliferative disorders
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous γδ T-cell lymphoma
- *Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma*
- *Primary cutaneous acral $CD8^+$ T-cell lymphoma**
- *Primary cutaneous $CD4^+$ small/medium T-cell lymphoproliferative disorder**
- Peripheral T-cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- *Follicular T-cell lymphoma**
- *Nodal peripheral T-cell lymphoma with TFH phenotype**
- Anaplastic large-cell lymphoma, ALK^+
- Anaplastic large-cell lymphoma, ALK^-*
- *Breast implant–associated anaplastic large-cell lymphoma**

Hodgkin lymphoma

- Nodular lymphocyte predominant Hodgkin lymphoma
- Classical Hodgkin lymphoma
  - Nodular sclerosis classical Hodgkin lymphoma
  - Lymphocyte-rich classical Hodgkin lymphoma
  - Mixed cellularity classical Hodgkin lymphoma
  - Lymphocyte-depleted classical Hodgkin lymphoma

Posttransplant lymphoproliferative disorders (PTLD)

- Plasmacytic hyperplasia PTLD
- Infectious mononucleosis PTLD
- Florid follicular hyperplasia PTLD*
- Polymorphic PTLD
- Monomorphic PTLD (B- and T-/NK-cell types)
- Classical Hodgkin lymphoma PTLD

Histiocytic and dendritic cell neoplasms

- Histiocytic sarcoma
- Langerhans cell histiocytosis
- Langerhans cell sarcoma
- Indeterminate dendritic cell tumor
- Interdigitating dendritic cell sarcoma
- Follicular dendritic cell sarcoma
- Fibroblastic reticular cell tumor
- Disseminated juvenile xanthogranuloma
- Erdheim-Chester disease*

« MLUS » ou MBL

- présence d'une lymphocytose B monoclonale avec lymphocytose totale < 5000/mm3 et absence de critères pour lymphome (pas d'adénopathies, ni splénomégalie, ni cytopénies)

- chez 4 à 5% des adultes ! et incidence en augmentation avec l'âge

- suivi annuel recommandé vu risque d'évolutive vers LLC 1 à 2% par an

- WHO 2016 :« low count MBL » < 0,5 G/L : pas de suivi nécessaire vs « high count MBL

Exemple : leucémie lymphoïde chronique

Définitions

	Lymphocytes B clonaux	Adénopathies/ organomégalie
LLC	> 5000/µl	±
Ly lymphocytique	< 5000/µl	+
Lymphocytose monoclonale	< 5000/µl	-

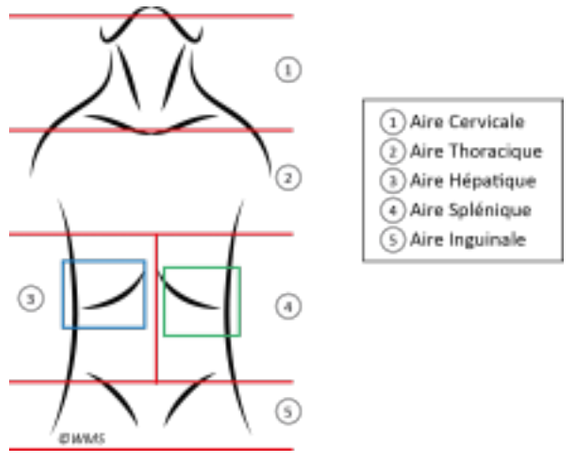
Hallek, Blood 2008; 111 : 5446

Matutes / Catovsky index

Marker	CLL	Score	Other B-cell leukemias	Score
SIg	weak	1	strong	0
CD5	positive	1	negative*	0
CD23	positive	1	negative	0
CD79b/CD22	weak	1	strong	0
FMC7	negative	1	positive	0
	CLL score 4-5		usual score 0-2	

* except mantle cell lymphoma

Stadification « pronostique »



CLL STAGING SYSTEMS

Rai System[a]

Stage	Description	Modified Risk Status
0	Lymphocytosis, lymphocytes in blood >5 x 10^9/L clonal B-cells and >40% lymphocytes in the bone marrow	Low
I	Stage 0 with enlarged node(s)	Intermediate
II	Stage 0–I with splenomegaly, hepatomegaly, or both	Intermediate
III[c]	Stage 0–II with hemoglobin <11.0 g/dL or hematocrit <33%	High
IV[c]	Stage 0–III with platelets <100,000/mcL	High

Binet System[b]

Stage	Description
A	Hemoglobin ≥10 g/dL and Platelets ≥100,000/mm^3 and <3 enlarged areas
B	Hemoglobin ≥10 g/dL and Platelets ≥100,000/mm^3 and ≥3 enlarged areas
C[c]	Hemoglobin <10 g/dL and/or Platelets <100,000/mm^3 and any number of enlarged areas

Evaluation pronostique : recommandations

PROGNOSTIC INFORMATION FOR CLL/SLL[a]

***TP53* and Immunoglobulin Heavy-Chain Variable (*IGHV*) Region Gene Mutation and Surrogates by Flow Cytometry**

	Favorable	Unfavorable
DNA sequencing[b]		
TP53	**Wild-type**	**Mutated**
IGHV	**>2% mutation**	**≤2% mutation**
Flow Cytometry[c]		
CD38	**<30%**	**≥30%**
Zap 70	**<20%**	**≥20%**
CD49d	**<30%**	**≥30%**

Interphase Cytogenetics (FISH)[d]

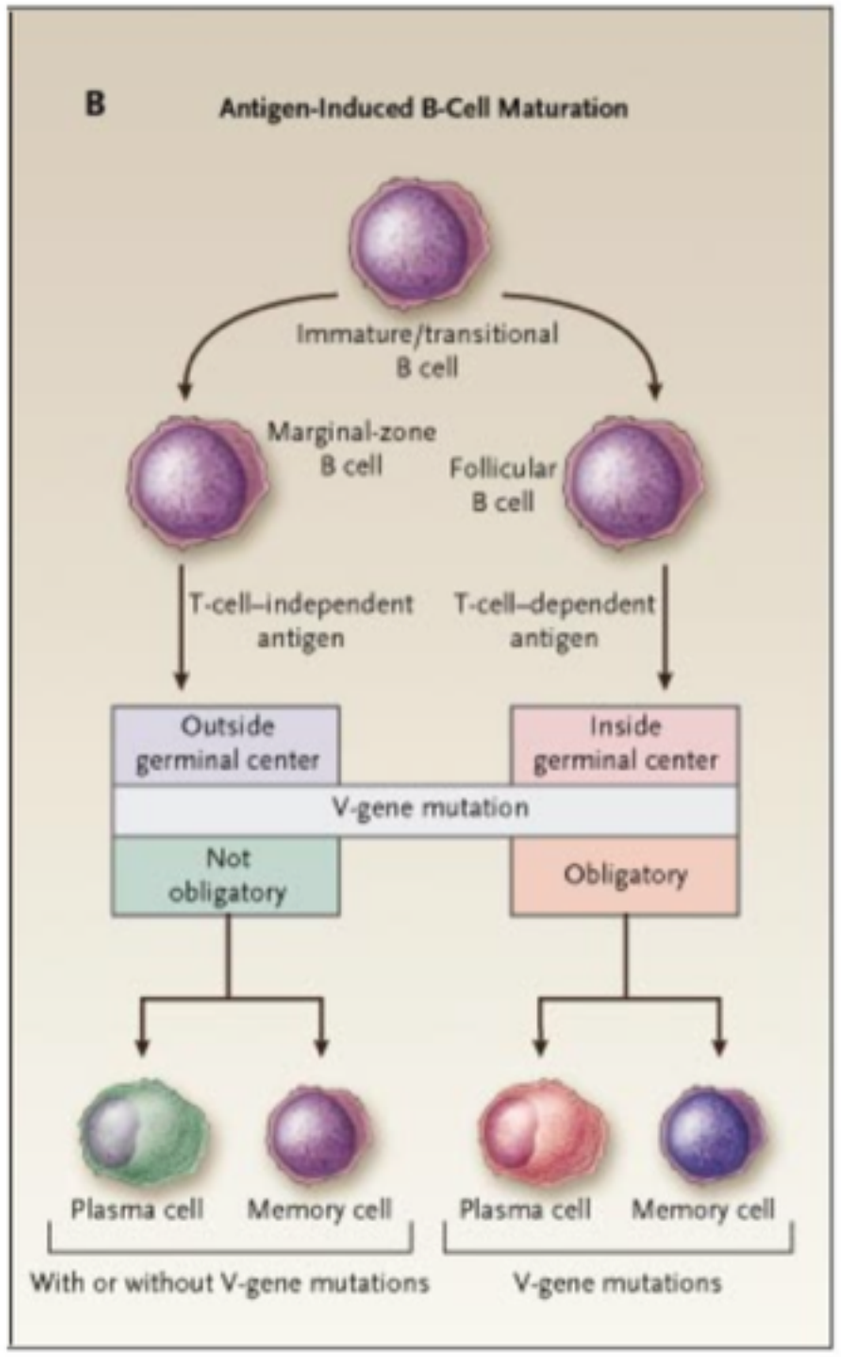
Unfavorable	Neutral	Favorable
del(11q) **del(17p)**	**Normal** **+12**	**del(13q) (as a sole abnormality)**

Complex karyotype[e]

Unfavorable
≥3 unrelated chromosome abnormalities in more than one cell on karyotype

[a]This table provides useful prognostic information relative to the time to progression, where therapy is required, and survival. The presence of del(11q) and/or del(1 are associated with short progression-free survival with chemotherapy and chemoimmunotherapy approaches.
[b]*IGHV* rearrangements involving VH3-21 carry a poor prognosis even if mutated. *TP53* mutation status also provides additional prognostic information to FISH.
[c]*IGHV* mutation status is preferred over flow cytometry. Flow cytometry markers may be surrogate markers for *IGHV* mutation status. If not available, determination CD38, CD49d, and ZAP-70 expression by flow cytometry may be used as a surrogate for *IGHV* mutation status. Evaluation of these markers can be challenging a not recommended outside the setting of a clinical trial.
[d]Formal studies identifying the percentage of abnormal cells identified by FISH are ongoing, although populations less than 10% appear to not have the clinical imp as noted in the table.
[e]Complex karyotype is based on results of conventional karyotyping of stimulated CLL cells.

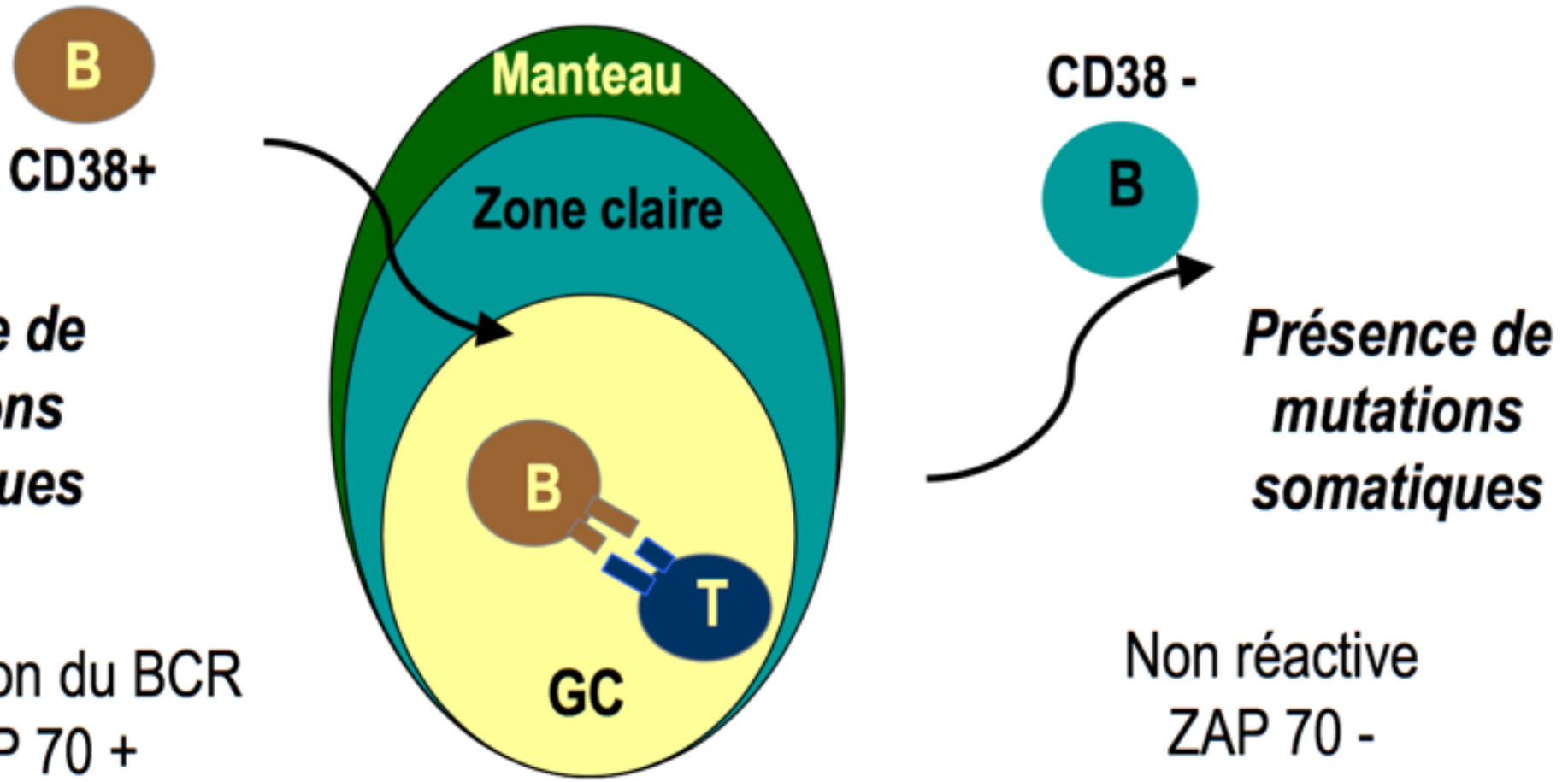
A Comparison of Pathways of B-Cell Maturation According to T-Cell Dependency



Chiorazzi N et al. N Engl J Med 2005;352:804-815

Statut Mutationnel des Ig

Deux Profils Evolutifs Différents



Absence de mutations somatiques

Activation du BCR
ZAP 70 +

Mauvais pronostic

Présence de mutations somatiques

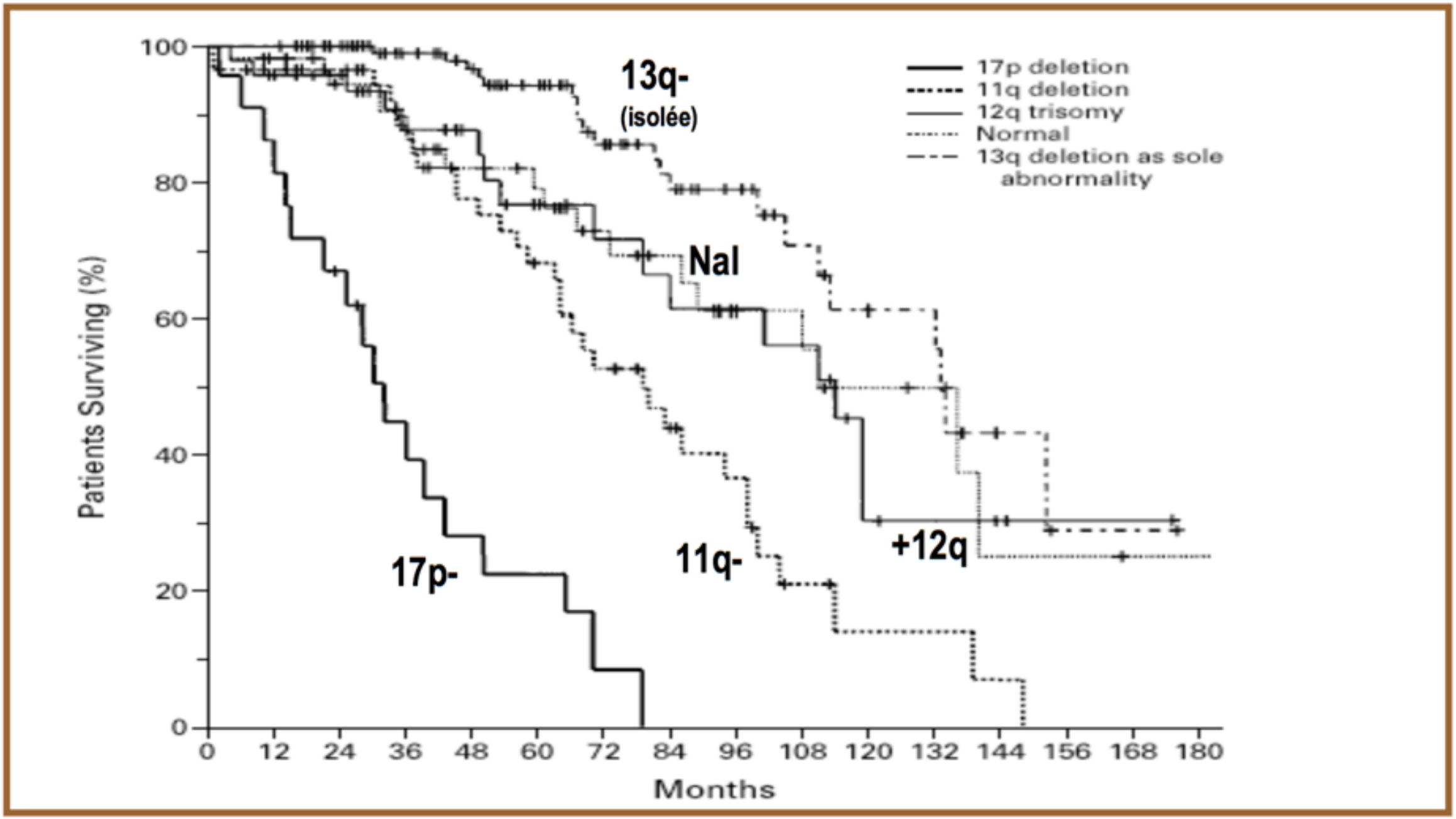
Non réactive
ZAP 70 -

Bon pronostic

Anomalies cytogénétiques

- **Présence d'anomalies génétiques dans près de 80% des cas**
  - **Délétion du 13q**
    - La plus fréquente, 50% des cas, bon pronostic si isolée
  - **Trisomie 12**
    - Environ 15% des cas, pronostic plutôt péjoratif,
    - Associé à cytologie atypique
  - **Délétion 11q**
    - 10% des cas, très mauvais pronostic,
    - Associé à des formes tumorales,
    - Ré-évolutivité rapide après traitement
  - **Délétion 17p**
    - Moins de 10% des cas, très mauvais pronostic,
    - p53 non fonctionnelle, résistance à la fludarabine
    - Ré-évolutivité rapide après traitement

Signification Pronostiques des Anomalies Chromosomiques, LLC-B



(1) Döhner, N Engl J Med,2000;343:1910

Résumé des Facteurs Pronostiques

Bon pronostic

- Stade A
- Pas de prolifération
  - Temps de doublement long
  - TK basse
- CD38 –
- Présence de mutations somatiques
- ZAP-70 –
- Del13 q ou absence d'anomalies cytogénétiques

Mauvais pronostic

- Stade B ou C
- Signes de prolifération
  - Temps de doublement court
  - TK élevée
- CD38 +
- Absence de mutations somatiques
- ZAP-70 +
- Del11 q, del17p, trisomie 12 ou autres anomalies cytogénétiques rares et caryotype complexe

Recommandations thérapeutiques

	Pratique courante	Essai clinique
Stade A	non	question expérimentale
Stade B	peut-être (si active)	peut-être (si active)
Stade C	oui	oui
Maladie active/ progressive	oui	oui
Maladie non progressive	non	question expérimentale

Hallek, Blood 2008; 111 : 5446

LLC : critères de maladie active/progressive

- Insuffisance médullaire progressive
- Splénomégalie massive (≥ 6 cm sous le rebord costal)
- Adénopathies massives (≥ 10 cm) ou progressives
- Temps de doublement lymphocytaire < 6 mois
- Anémie/thrombopénie auto-immunes ne répondant pas aux corticoïdes
- Symptômes "B"
  - amaigrissement, fièvre, sueurs nocturnes
  - fatigue (ECOG ≥ 2)

<u>NB</u> : le nombre de lymphocytes n'est pas à lui seul un critère de traitement

Hallek, Blood 2008; 111 : 5446

Quels projets thérapeutiques en 1ère ligne pour les stades B et C

Option liée à l'âge

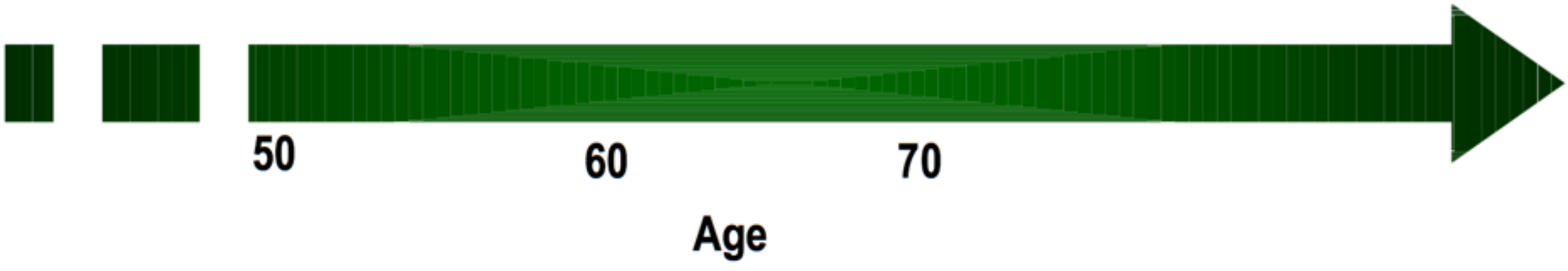
Meilleure réponse globale et meilleure survie sans traitement

Option potentiellement curative par intensification avec recours aux greffes de CSP auto ou allogreffe

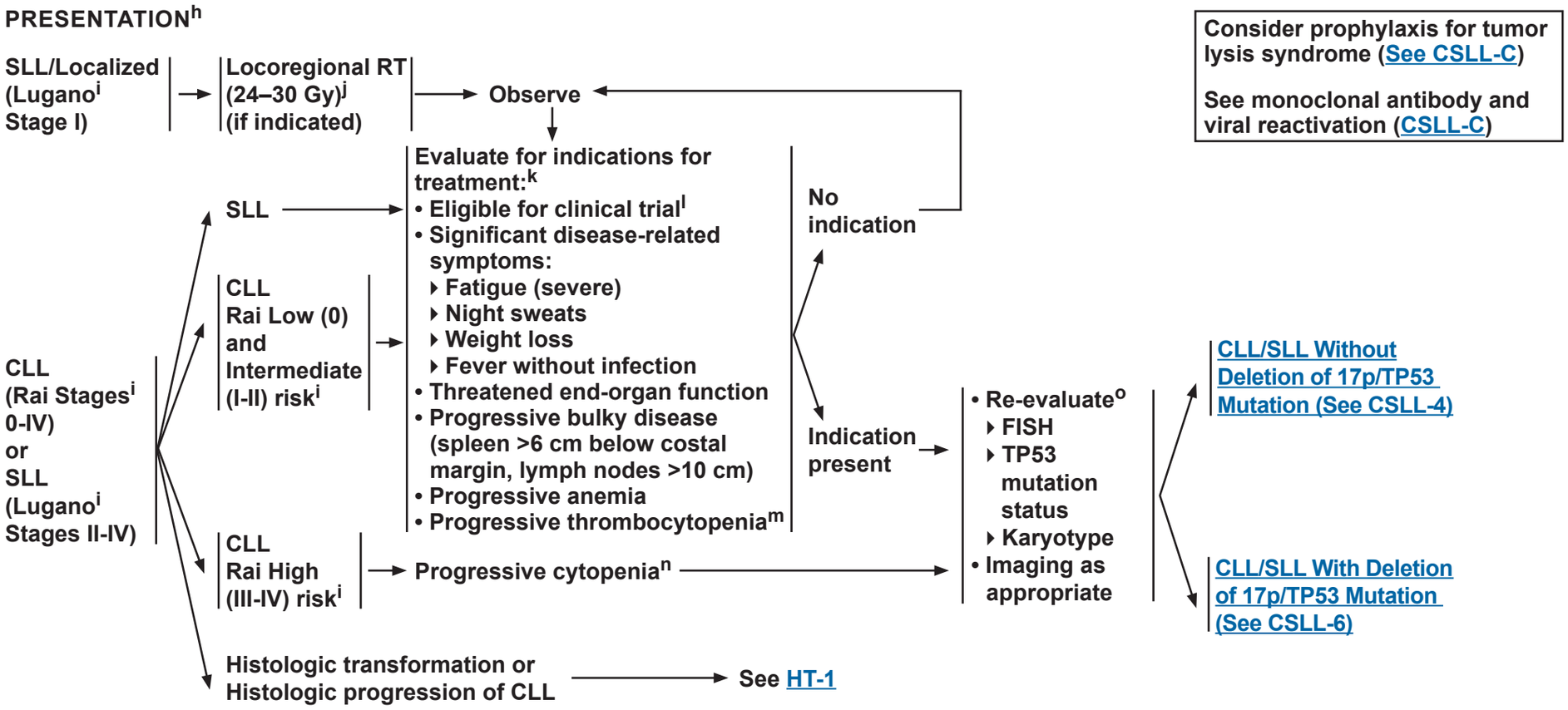
Meilleure survie sans traitement

Qualité de vie

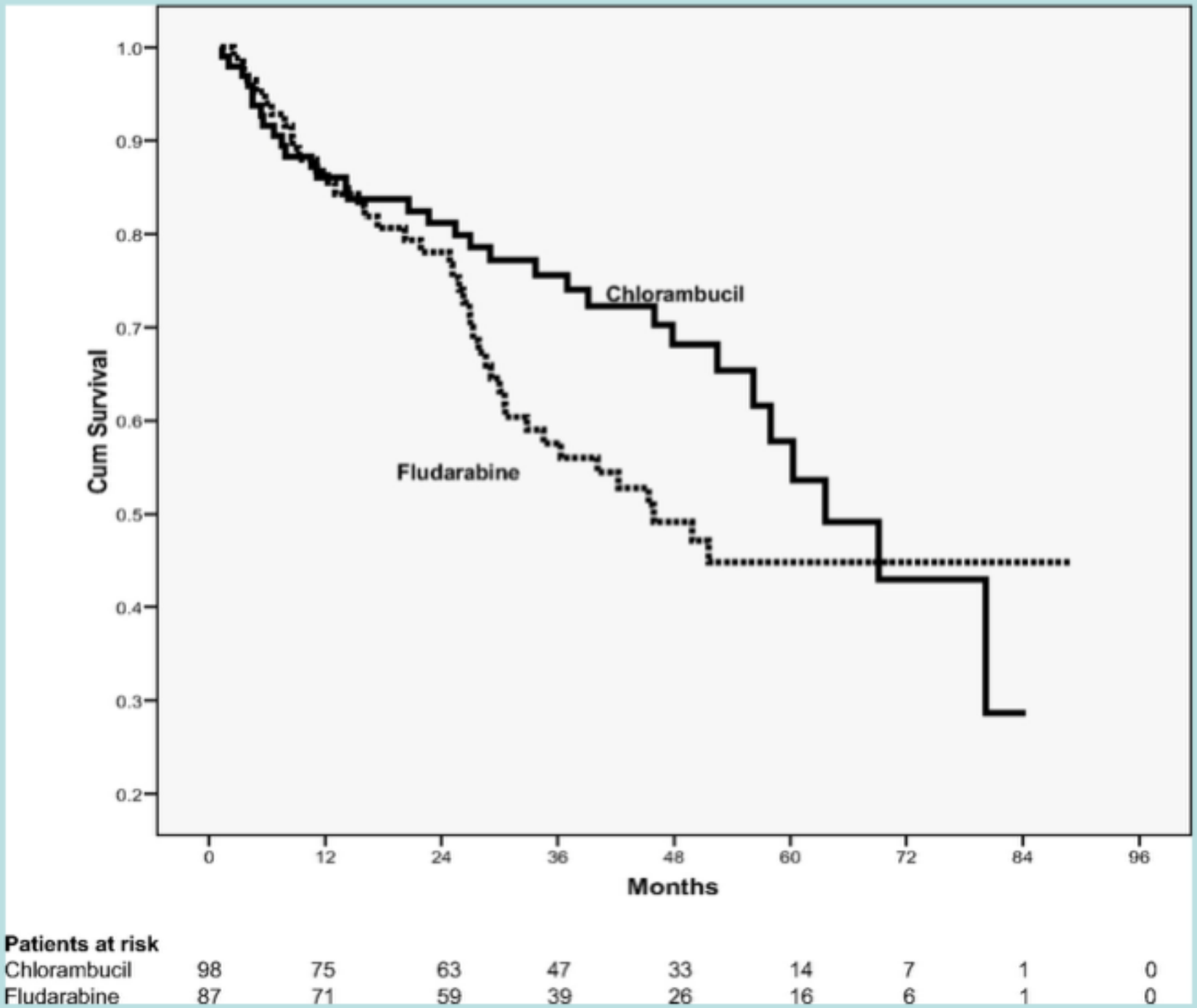
Qualité de vie



En 2018?

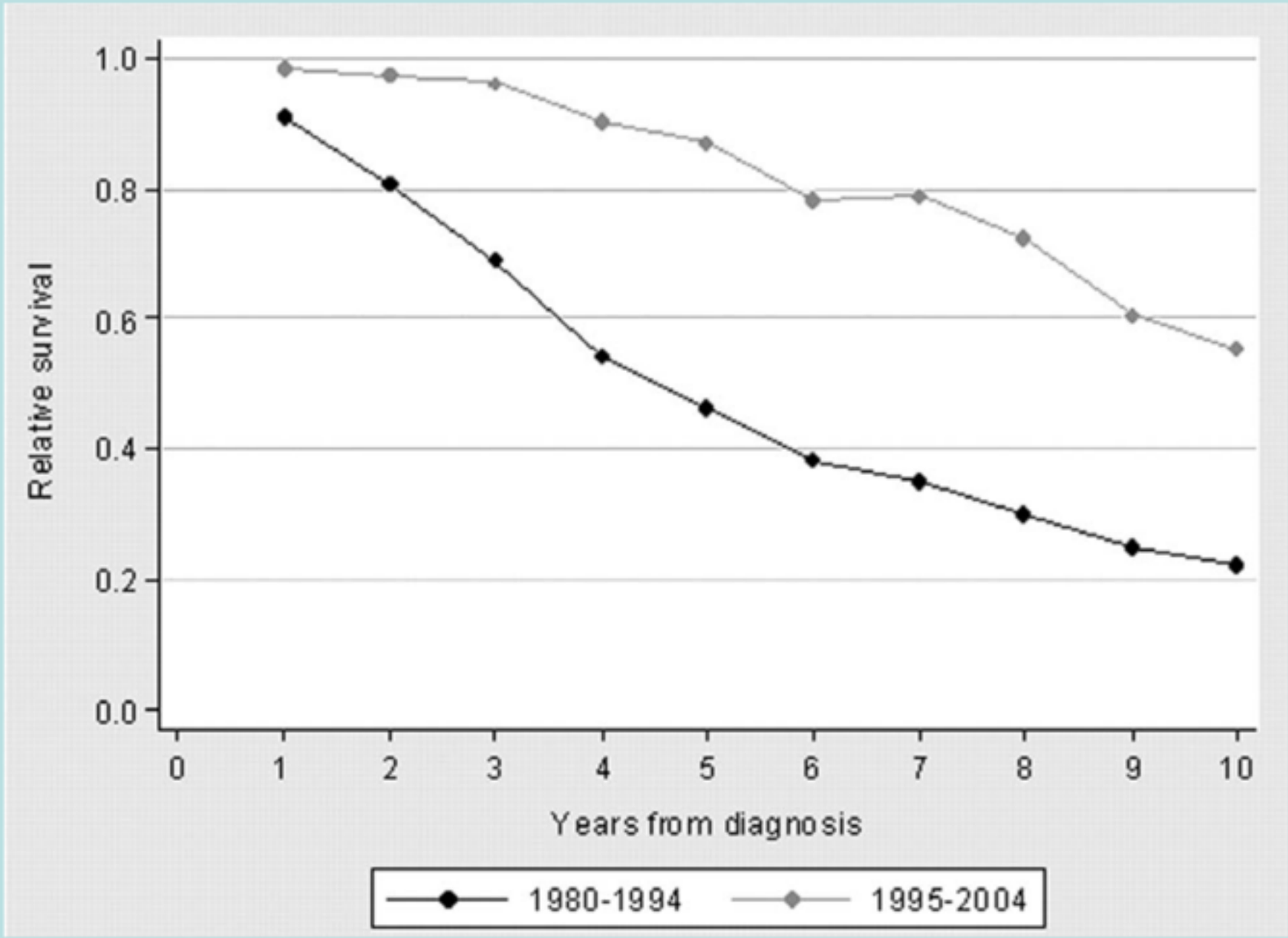

PRESENTATION[h]
SLL/Localized (Lugano[i] Stage I)
Locoregional RT (24–30 Gy)[j] (if indicated)
Observe
Evaluate for indications for treatment:[k]
• Eligible for clinical trial[l]
• Significant disease-related symptoms:
▸ Fatigue (severe)
▸ Night sweats
▸ Weight loss
▸ Fever without infection
• Threatened end-organ function
• Progressive bulky disease (spleen >6 cm below costal margin, lymph nodes >10 cm)
• Progressive anemia
• Progressive thrombocytopenia[m]
No indication
Indication present
CLL (Rai Stages[i] 0-IV) or SLL (Lugano[i] Stages II-IV)
SLL
CLL Rai Low (0) and Intermediate (I-II) risk[i]
CLL Rai High (III-IV) risk[i]
Progressive cytopenia[n]
• Re-evaluate[o]
▸ FISH
▸ TP53 mutation status
▸ Karyotype
• Imaging as appropriate
CLL/SLL Without Deletion of 17p/TP53 Mutation (See CSLL-4)
CLL/SLL With Deletion of 17p/TP53 Mutation (See CSLL-6)
Histologic transformation or Histologic progression of CLL
See HT-1
Consider prophylaxis for tumor lysis syndrome (See CSLL-C)
See monoclonal antibody and viral reactivation (CSLL-C)

Elderly patients : Overall survival according to randomization



Eichhorst, B. F. et al. Blood 2009;114:3382-3391

Ten-year relative survival curves for patients younger than 70 years in Binet stage B/C according to whether they were diagnosed in the calendar periods 1980-1994 or 1995-2004



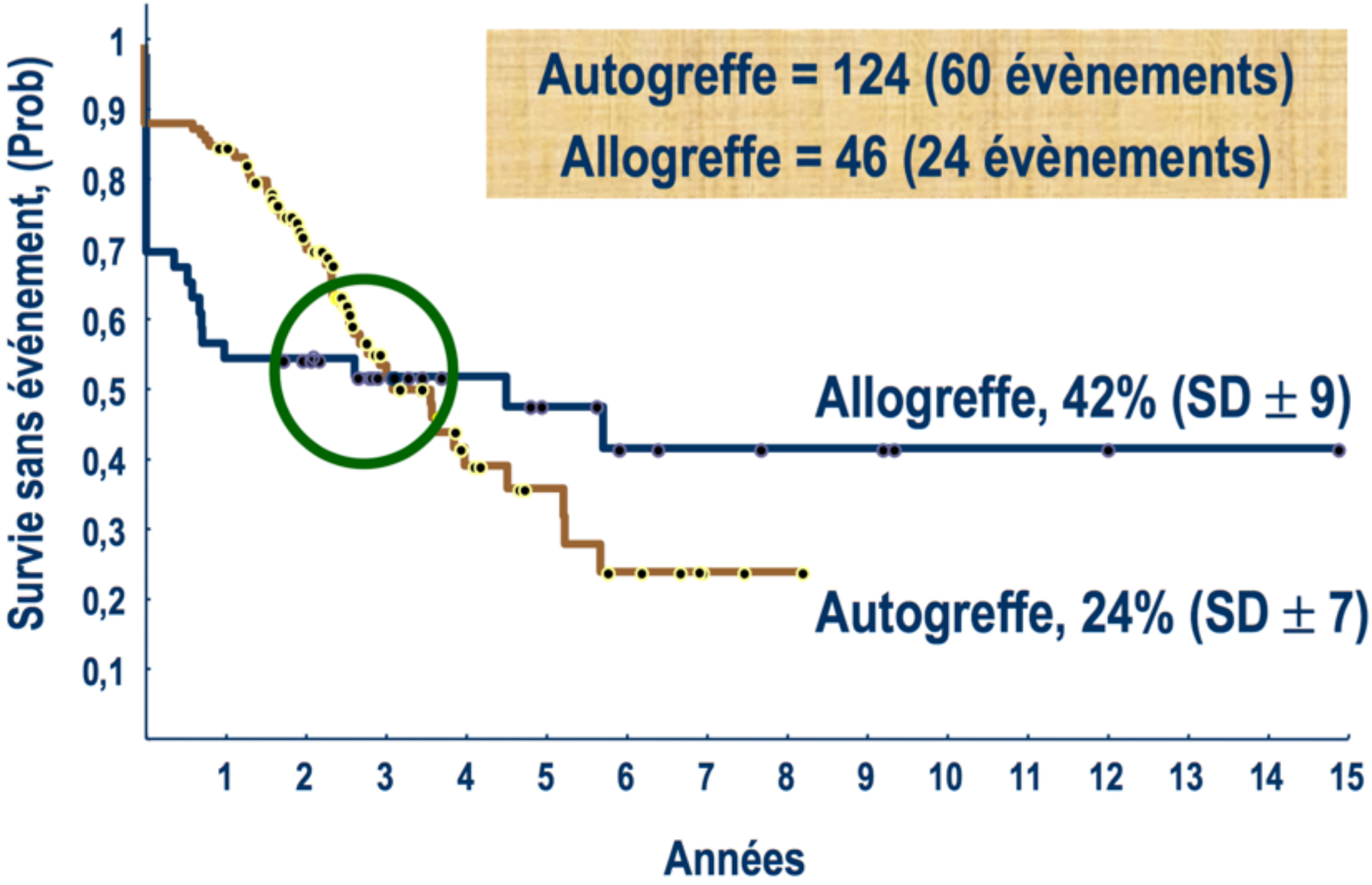
Abrisqueta, P. et al. Blood 2009;114:2044-2050

Rituximab Fludarabine Cyclophosphamide

	n	CR %	OR %	Survival/ duration response
Phase II Keating	224	70	95	TTF 69 % (at 4 years)
Phase III Hallek	871	52	95	PFS 76.6 % OS 91 %
RFC vs FC		27	88	62.3 % 88 %

Ricci, Ther Clin Risk Management 2009; 5 : 187

Survie sans événement (1)



(1) Esteve J, Blood, 2002;99:1873-4

Non myelo-ablative SCT in CLL

n	Age	% CR	% TRM	% prog.	% survival
294	50-57 (12-73)	40-78	6-26	7-48	78-80

Tam C.S. and Khouri I, Hematol Oncol 2009; 27 : 53

En 2008

LLC :Algorithmes de traitement

	< 65 ou 70 ans	≥ 65-70 ans
• **"Gold standard"**	R Rituximab F Fludarabine C Cyclophosphamide	Chlorambucil
• **17 p⁻**	Alemtuzumab Greffe allogénique	Alemtuzumab
• **Rechutes/réfractaires Situations particulières**	RFC, Alemtuzumab, Bendamustine, Ofatumumab, anti-BCL-2, Cyclosporine, Flavopiridol, greffe allogénique, greffe autologue	Fludarabine, Rituximab-F, F-C, Ofatumumab, Bendamustine, Lenalidomide

LLC :Algorithmes de traitement

	< 65 ou 70 ans	≥ 65-70 ans
• **"Gold standard"**	R Rituximab F Fludarabine C Cyclophosphamide	Chlorambucil
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aujourd’hui?

- Nouvelles données avec « vieilles » molécules
- Monoclonaux de nouvelle génération (GA-101)
- Nouvelles classes thérapeutiques
  - inhibiteurs de la Bruton tyrosine kinase
  - inhibiteurs bcl-2
  - …
- Associations

Traitement de 1e ligne actuel de la LLC

<table>
<tr><th>Stade</th><th>État général</th><th>del(17p)
p53mut</th><th>Traitement</th></tr>
<tr><td>Binet A-B
non active</td><td>Non applicable</td><td>Non applicable</td><td>Aucun</td></tr>
<tr><td rowspan="3">Maladie active ou
Binet C</td><td rowspan="2">Go go</td><td>Non</td><td>FCR</td></tr>
<tr><td>Oui</td><td>Allogreffe (?)</td></tr>
<tr><td rowspan="2">Slow go</td><td>Non</td><td>CLB + Ac mo anti-CD20 (GA-101)</td></tr>
<tr><td>Oui</td><td>Ibrutinib, alemtuzumab, rituximab ou ofatumumab à fortes doses</td></tr>
</table>

Traitement de 2e ligne de la LLC

Réponse au traitement de 1re ligne	État général	Traitement	
		Standard	Alternatives (essais)
Maladie réfractaire ou en progression dans les 2 ans	Go go	Alemtuzumab + dexa, FA, FCR, ibrutinib puis allogreffe (?)	Lénalidomide, BR, (inhibiteurs de kinase, inhibiteur de Bcl-2)
	Slow go	Changer de traitement (si possible essai clinique)	Ibrutinib, idélalisib + rituximab, alemtuzumab pour les del(17p), FCR-lite, BR, lénalidomide, ofatumumab, rituximab à fortes doses
Progression après 2 ans	Tous	Répéter le traitement de 1re ligne	

EHA 2014 - D'après Hallek M, session éducationnelle LLC

Stratégies thérapeutiques « futures » pour obtenir un contrôle de la maladie à long terme : schéma « séquentiel triple T » Tailored, Targeted, Total eradication of MRD

Debulking	Induction (associations)	Entretien en fonction de la MRD (agents en monothérapie)
• Chimiothérapie non intensive : bendamustine ou fludarabine	• Inhibiteurs de kinase • Anticorps monoclonaux • Inhibiteur de Bcl2	• Anticorps monoclonaux • Lénalidomide Inhibiteurs de kinase • Inhibiteur de Bcl2
1-2 mois (1-2 cycles)	6-12 mois	1 an - ∞

EHA 2014 - D'après Hallek M, session éducationnelle LLC

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- 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**
- Burkitt lymphoma
- *Burkitt-like lymphoma with 11q aberration**
- High-grade B-cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements*
- High-grade B-cell lymphoma, NOS*
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

Mature T and NK neoplasms

- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- *Chronic lymphoproliferative disorder of NK cells*
- Aggressive NK-cell leukemia
- Systemic EBV^+ T-cell lymphoma of childhood*
- Hydroa vacciniforme–like lymphoproliferative disorder*
- Adult T-cell leukemia/lymphoma
- Extranodal NK-/T-cell lymphoma, nasal type
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma*
- *Indolent T-cell lymphoproliferative disorder of the GI tract**
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous $CD30^+$ T-cell lymphoproliferative disorders
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous γδ T-cell lymphoma
- *Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma*
- *Primary cutaneous acral $CD8^+$ T-cell lymphoma**
- *Primary cutaneous $CD4^+$ small/medium T-cell lymphoproliferative disorder**
- Peripheral T-cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- *Follicular T-cell lymphoma**
- *Nodal peripheral T-cell lymphoma with TFH phenotype**
- Anaplastic large-cell lymphoma, ALK^+
- Anaplastic large-cell lymphoma, ALK^-*
- *Breast implant–associated anaplastic large-cell lymphoma**

Hodgkin lymphoma

- Nodular lymphocyte predominant Hodgkin lymphoma
- Classical Hodgkin lymphoma
  - Nodular sclerosis classical Hodgkin lymphoma
  - Lymphocyte-rich classical Hodgkin lymphoma
  - Mixed cellularity classical Hodgkin lymphoma
  - Lymphocyte-depleted classical Hodgkin lymphoma

Posttransplant lymphoproliferative disorders (PTLD)

- Plasmacytic hyperplasia PTLD
- Infectious mononucleosis PTLD
- Florid follicular hyperplasia PTLD*
- Polymorphic PTLD
- Monomorphic PTLD (B- and T-/NK-cell types)
- Classical Hodgkin lymphoma PTLD

Histiocytic and dendritic cell neoplasms

- Histiocytic sarcoma
- Langerhans cell histiocytosis
- Langerhans cell sarcoma
- Indeterminate dendritic cell tumor
- Interdigitating dendritic cell sarcoma
- Follicular dendritic cell sarcoma
- Fibroblastic reticular cell tumor
- Disseminated juvenile xanthogranuloma
- Erdheim-Chester disease*

Autre exemple?

- L’histoire de Mr D, 38 ans LAIT
  - angine avec adénopathies cervicales trainantes
  - prurit ++, diarrhées…
  - discrète lymphocytose, TCR réarrangé

Merci pour votre attention !