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Accuracy of diagnostic methods and impact on clinical management : The Lymphopath Network experience

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Lymphomas: the French experience ...

- **LYSA :**
 - multicentric clinical group in 2012 (merging of former GELA & GOELAMS groups)
 - LYSA-pathology : clinical trials based on histological subtypes
 - ~only 10-15% of lymphoma patients
- **LYMPHOPATH :**
 - pathology network for **all** lymphoma patients
 - labelled by INCa (NCI)
- **Molecular platforms :**
 - performing molecular theranostic tests (solid tumours,....)
 - labelled by INCa (NCI)

Background

- More than 80 lymphoma entities in the WHO 2017 classification
 - Lymphoma diagnosis is challenging: expertise, ancillary tools
 - An accurate diagnosis is critical for the clinical management of lymphoma patients
 - A few rather “limited” studies (in USA and in UK) have reported a variable discordance rate (6-28%) between referral and expert lymphoma diagnosis and a variable impact on patient care (2-17%)
- ***Lymphopath 2010 (INCa) : Realtime expert review of any newly diagnosed or suspected lymphomas***
- **Improve the clinical management of patients**
 - Lymphoma epidemiology
 - Facilitate research studies on lymphomas (LYSA)

Wilkins SB. *J Clin Pathol* 2011; Jaffe ES. *JCO* 2014

Lester *BHJ* 2003; Manion *Am J surg Pathol* 2008; LaCasce *JCO* 200;
Proctor *JCO* 2011; Matasar *Ann Oncol* 2012; Bowen *BJH* 2014



Lymphopath network

- **Review of any newly or suspected lymphoma diagnosis** by an expert hematopathologist
 - 42145 samples received during 2010-2013 period
 - 79754 cases (67621 lymphomas), 2010-2016
- **Expert pathologists with unlimited access** to ancillary techniques
- **Database recording both referral and expert diagnosis**
- **Rate of diagnostic changes («concordance/discordance»):**
 - % of submitted referral diagnosis confirmed or not by expert
 - cases sent for validation/cases sent for expertise
- **Major or minor changes classified by clinician according to their potential impact on clinical management**

30-33 expert sites
(University hospitals,
Comprehensive cancer centres)





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ORIGINAL REPORT

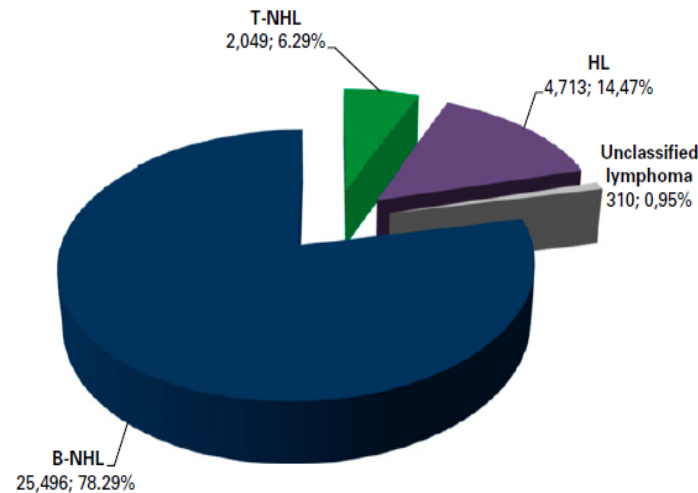
Impact of Expert Pathologic Review of Lymphoma Diagnosis: Study of Patients From the French Lymphopath Network

Camille Laurent, Marine Baron, Nadia Amara, Corinne Haioun, Mylène Dandoit, Marc Maynadié, Marie Parrens, Beatrice Vergier, Christiane Copie-Bergman, Bettina Fabiani, Alexandra Traverse-Glehen, Nicole Brousse, Marie-Christine Copin, Patrick Tas, Tony Petrella, Marie-Christine Rousselet, Josette Brière, Frédéric Charlotte, Catherine Chassagne-Clement, Thérèse Rousset, Luc Xerri, Anne Moreau, Antoine Martin, Diane Damotte, Peggy Dartigues, Isabelle Soubeyran, Michel Peoch, Pierre Dechelotte, Jean-François Michiels, Antoine de Mascarel, Françoise Berger, Céline Bossard, Flavie Arbion, Isabelle Quintin-Roué, Jean-Michel Picquenot, Martine Patey, Blandine Fabre, Henri Sevestre, Cécile Le Naoures, Marie-Pierre Chenard-Neu, Claire Bastien, Sylvie Thiebault, Laurent Martin, Manuela Delage, Thomas Filleron, Gilles Salles, Thierry Jo Molina, Georges Delsol, Pierre Brousset, and Philippe Gaulard

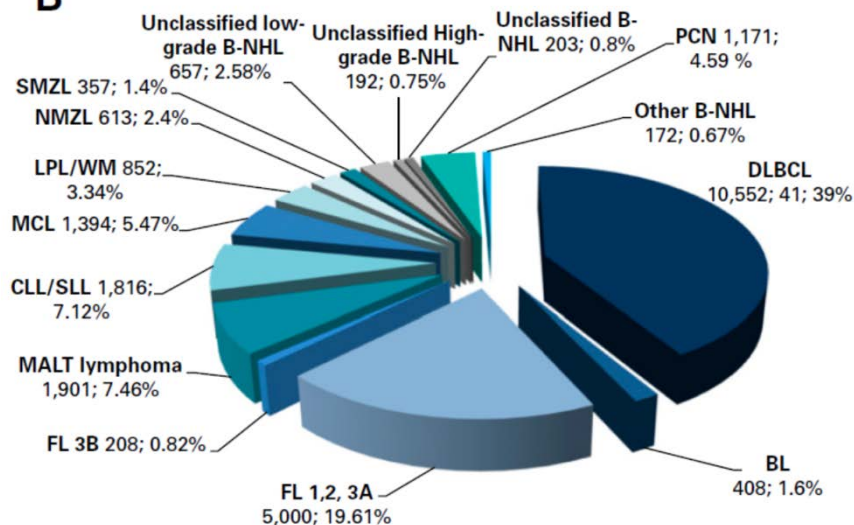
Main lymphomas categories in France (2010-2013) (42145 Samples, 36920 mature lymphomas)

Non-cutaneous lymphomas (n=32568)

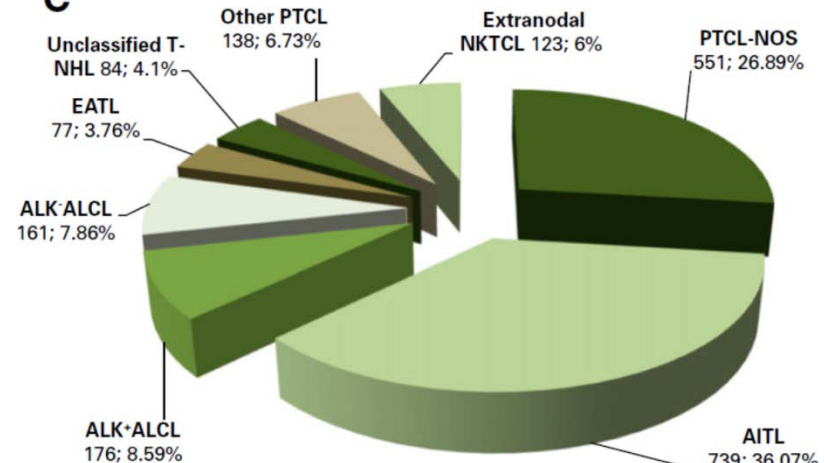
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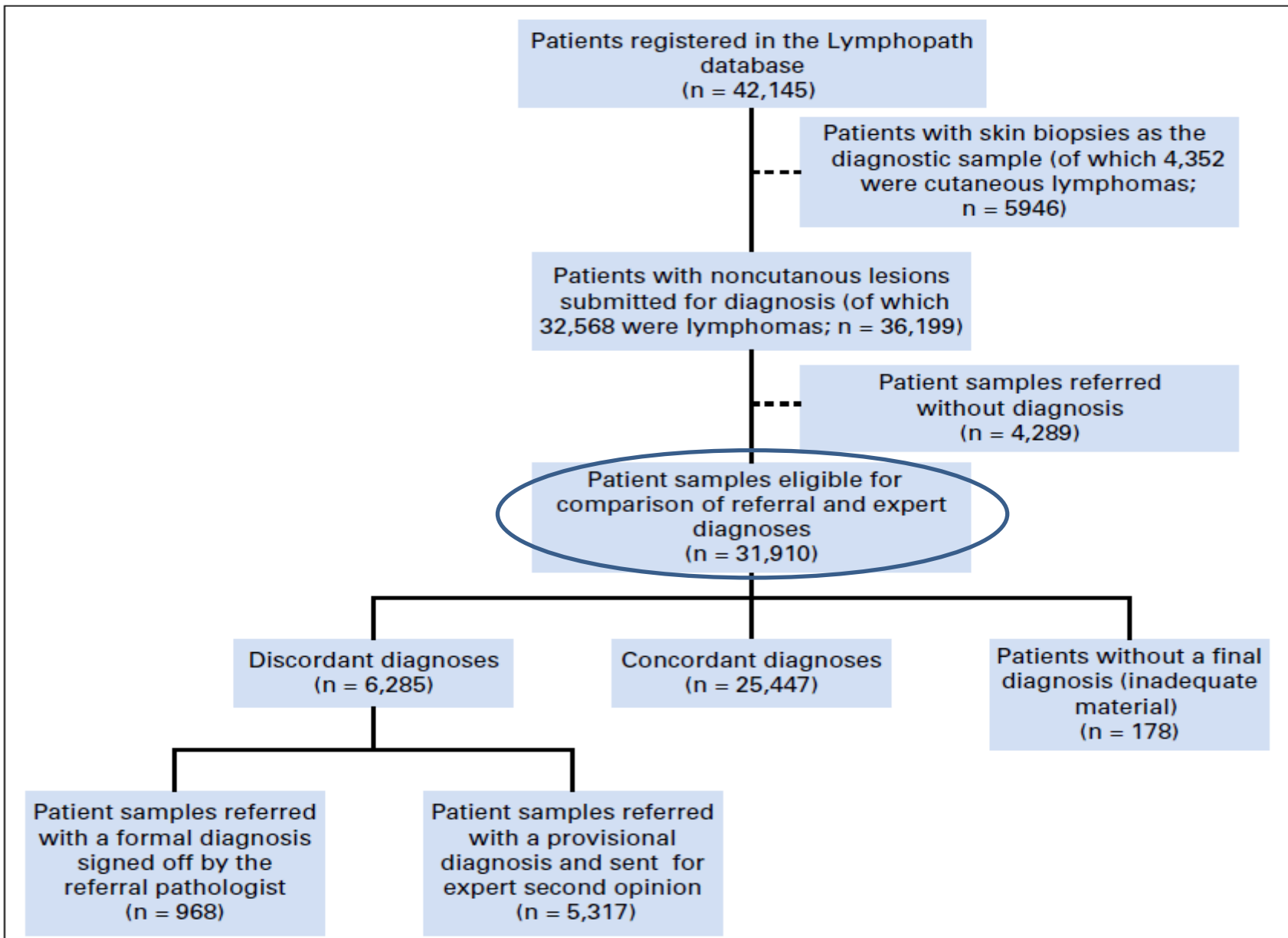
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Flowchart of the *Lymphopath* Study (2010-2013)





***Lymphopath* : overall diagnostic changes, 19.7%**

(°) 4289 pts submitted without diagnosis are excluded



***Lymphopath* : overall diagnostic changes, 19.7%**

- ✓ Patients sent with provisional diagnosis but seeking expert second opinion

n=19112, 37.8%

- ✓ Patients sent with formal diagnosis

n= 12798, 3.7% (°°)

(°) 4289 pts submitted without diagnosis are excluded

(°°) ~8% when internal cases are excluded

Quality control 319 randomly selected cases among expert sites: 99.05% concordance



Changes in cases with submitted diagnosis

Types of discordances :

Major discordances

Misclassification of lymphoma subtype

41.3%

Main lymphoma category misclassification

36.6%

Unclassified to classified lymphoma

Benign proliferation versus lymphoma

7.4%

Lymphoma versus another neoplasm

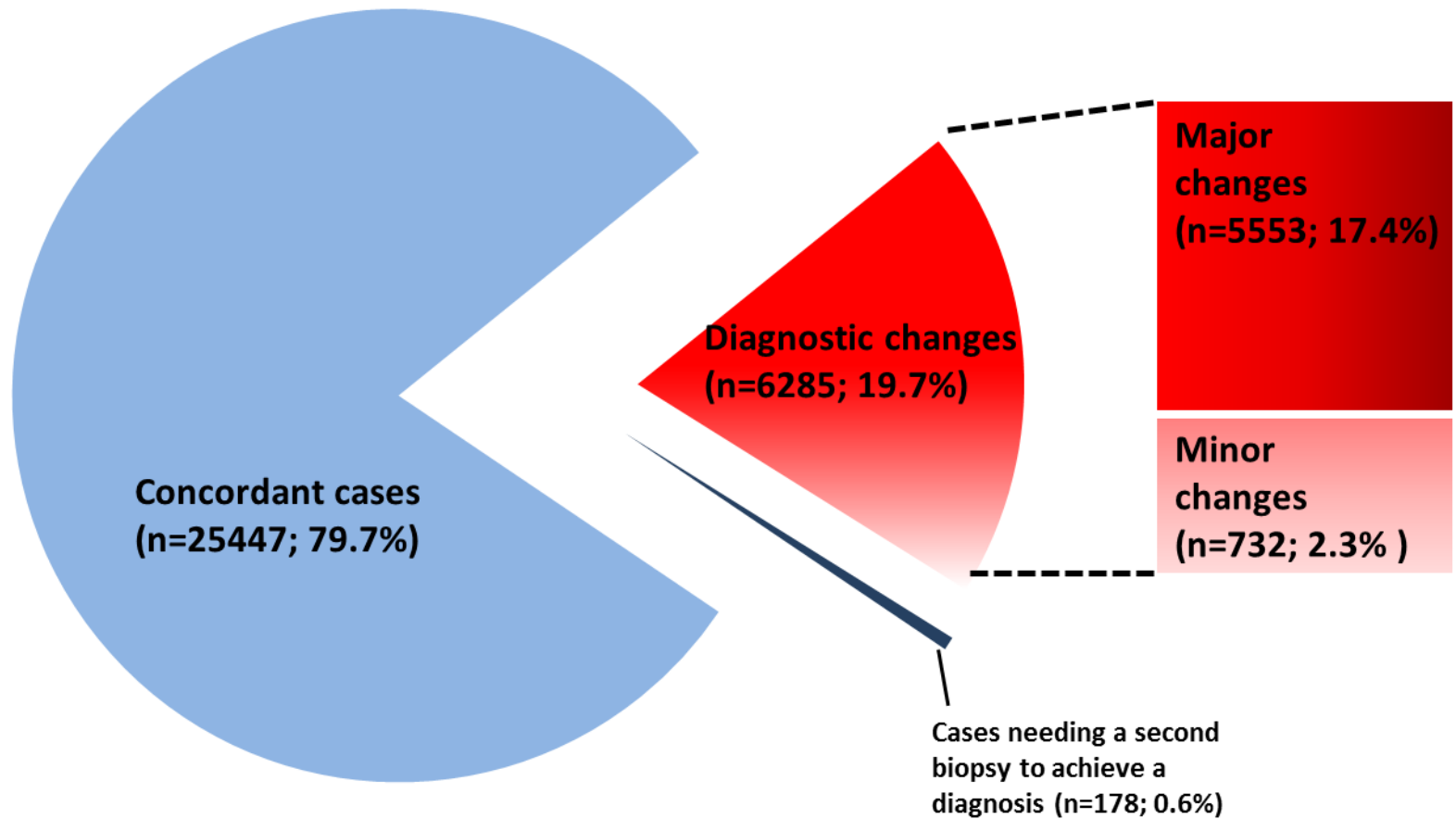
3%

Minor discordances

lymphoma subtype misclassification without change on patient care

11.7%

Schematic representation of the rates of concordances and changes between 31910 referral and expert diagnoses





Conclusions

1. Review of **67,829 newly diagnosed lymphoma cases** (2010 to 2015)
2. Confirmation of the initial diagnosis in ~80% of the patients
3. **Estimated clinical impact in ~17% of lymphoma patients**
4. Response time : 8 days
5. **Acces of every patient to specialized techniques** when needed
6. Training of pathologists and clinician involved in the management of the patients (diagnostic algorithms, meetings, website,....)
7. **Unique lymphoma database** in France:
 - useful for research studies
 - health monitoring: ***Exemple of the Bi-ALCL***
8. Ongoing:
 - evaluation of the referral labs/pathologists, « easy » situations
 - medico-economic evaluation
 - molecular assessment: introduction of new biomarkers, ex: RT3
 - clinical annotations : « real life » patients (REALYSA project)

Lymphopath: advantages & limits

Pro

- **Clinical impact (→ clinical trials, real life data, biomarkers...)**
- Absence of financial concern between pathologists
- All pathology labs (480)
- Solve the pb of 2d opinion
- Epidemiological survey
- Probably cost-effective
- The patients..!
- Health monitoring: Bi-ALCL..!

Cons

- Not all cases (~80%?)
- No clinical annotations
- Very unequal activity in the expert sites, difficulty to manage this increased activity in a difficult context
- « Feeling » from (some) referral pathologists



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LYSA – RT3 study

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