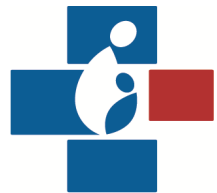




# Characterization and outcome of Pediatric lymphomas : 7 year experience of a single center in northern Uganda



ST MARY'S HOSPITAL  
**LACOR**

*Valeria Calbi, MD*  
**St MARY HOSPITAL, LACOR -UGANDA**



What can we learn from Africa?  
New insight to lymphoma classification,  
epidemiology, biology and research  
Paris, 9 – 10 May 2011

## The site



St Mary's Hospital Lacor is located in Gulu, North Uganda, is a Catholic mission hospital established in 1959 with 476 beds, 280,000 treated patients annually, it is the 3rd largest hospital in the country, offering general and specialized services to people living within 100 mile radius



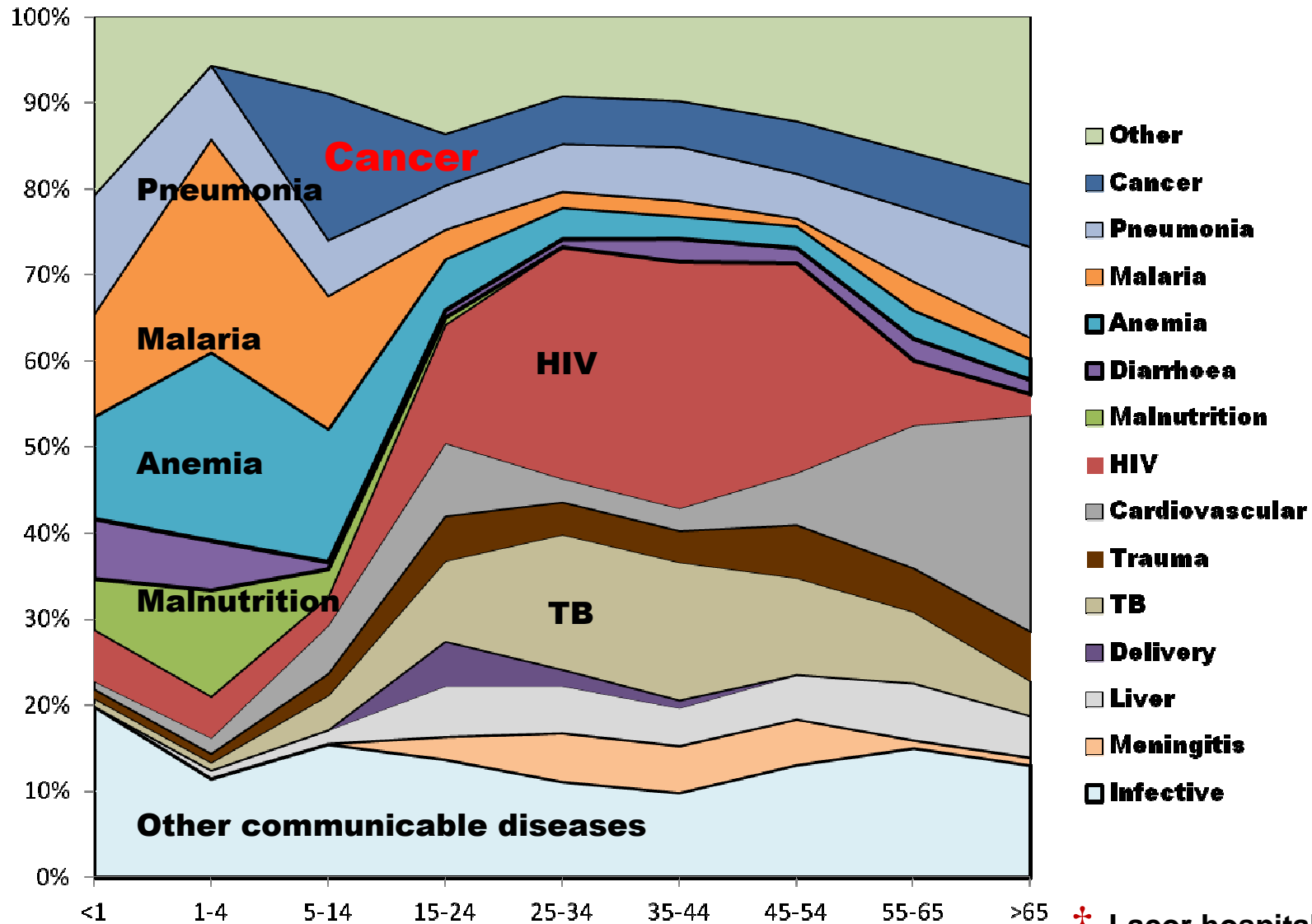
## The site

- ❖ majority of the people still live in mud-huts within small villages with no access to running water or electricity.
- ❖ There is limited access to hospitals due to bad road conditions and the absence of affordable public transportation



# Mortality Rate per Age 2008-2009 <sup>†</sup>

Cancer: first cause of death 5-14 yrs → 21%



<sup>†</sup> Lacor hospital data

# How to improve prognosis of the cancer

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**1.Diagnostic Capacity**

**2.Standardize clinical practice**

# How to improve prognosis of the cancer

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## 1.Diagnostic Capacity

## 2.Standardize clinical practice

### ❖ Background

An histopathology unit was established in St Mary's Hospital Lacor since 80's.

Until 2007 the slides were prepared by the hospital and sent to a senior pathologist in Kampala for the final diagnosis

n.45 BL cases between 1993-2007 have been reviewed by outside pathology with a diagnostic accuracy of 82% (37 confirmed of 45)

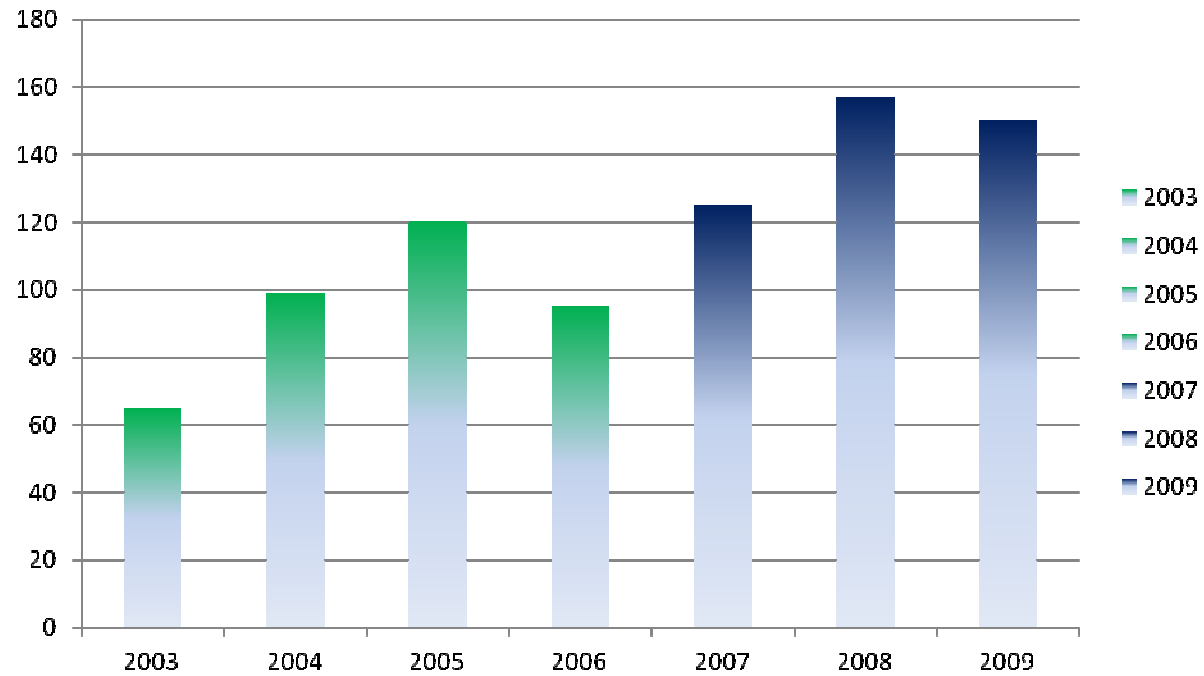
(Martin D. Ogwang et al. Arch Pathol Lab Med 135: 445-450)

### ❖ 2008

Since 2008 collaboration with Pathologists without Borders (APOF)

- sending pathologists on rotational basis
  - upgrade the unit
- Improving diagnostic strategy: cytology→histology

## Pediatric Cancer cases

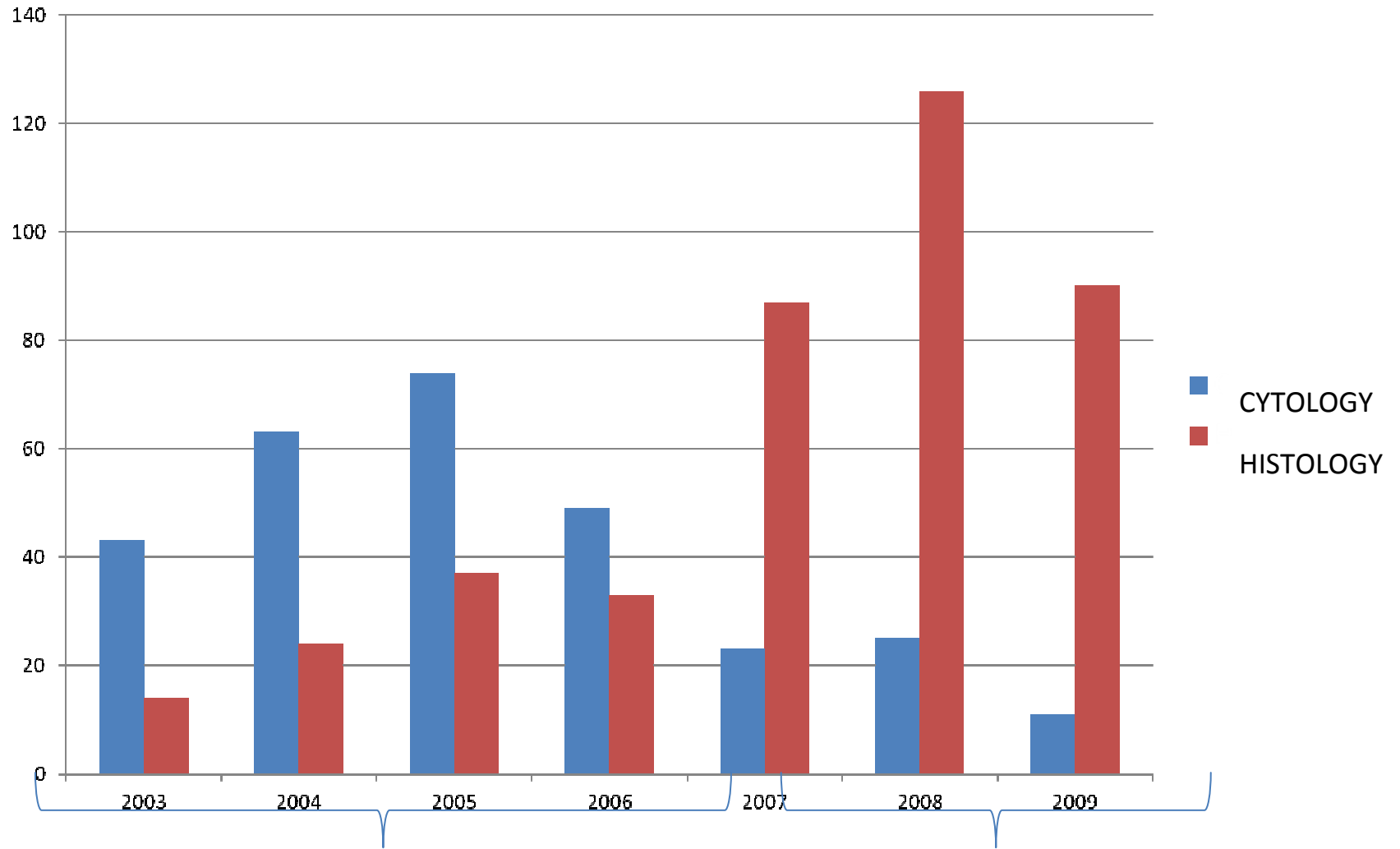


year	2003	2004	2005	2006	2007	2008	2009
N.	65	99	120	95	125	<b>157</b>	<b>150</b>

# Cytology

VS

# Tru-cut Biopsy

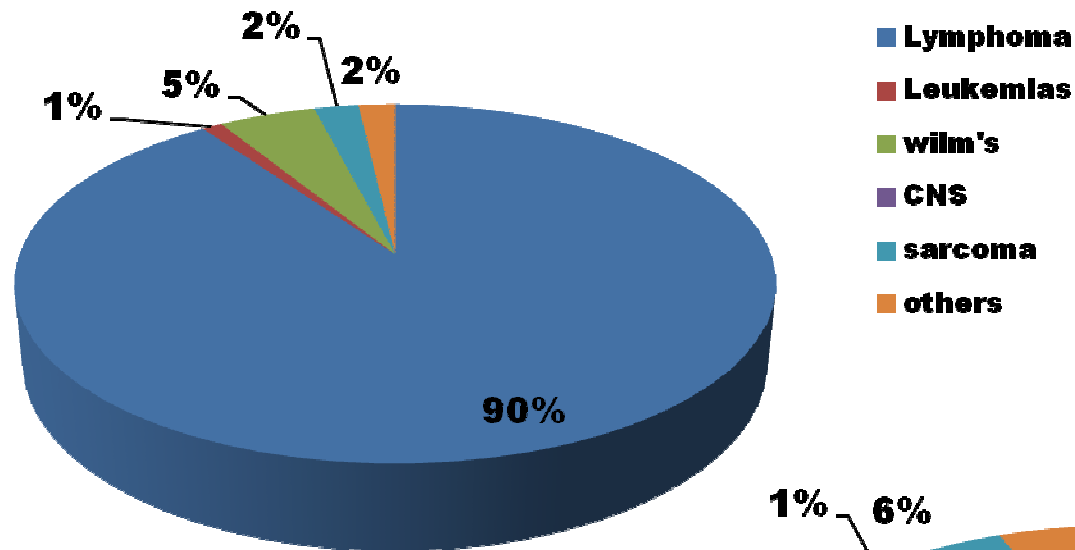


mean time for diagnosis: 1 month

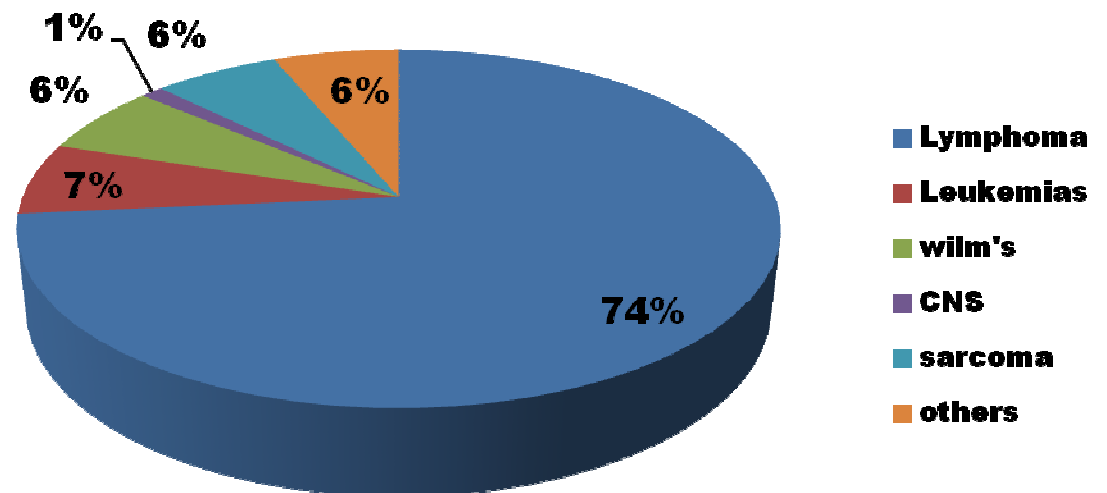
mean time for diagnosis: 5 days

# HAEMATHOLOGICAL vs NON-HAEMATHOLOICAL PEDIATRIC MALIGNANCIES

**2003-2007**

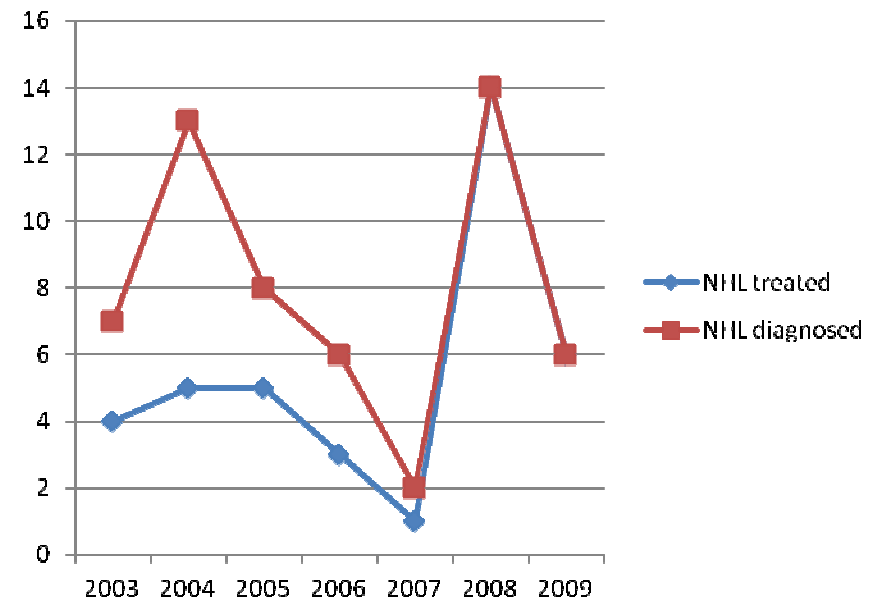
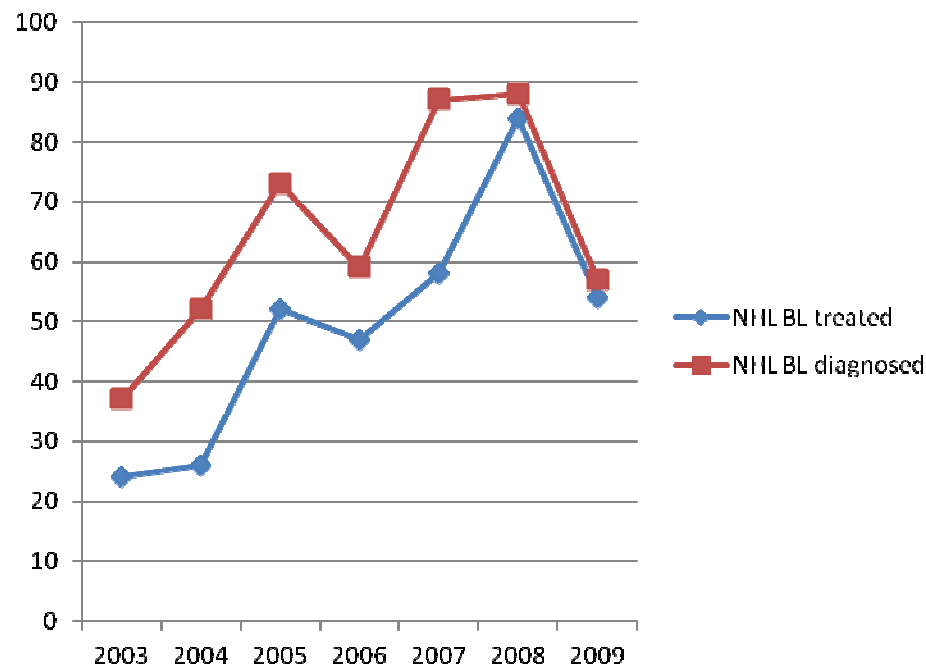


**2008-2010**



## Outcome

In the past 2 years almost all patients with a morphological diagnosis of BL or NHL have been evaluated and treated.



## Conclusions

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1. The impact of childhood lymphoproliferative disorders is high among curable-non communicable diseases.
2. The diagnosis based on morphology alone doesn't include many entities. Without accurate diagnosis effective patient management is not possible.
3. Improve diagnosis of lymphomas and lymphoproliferative disorders with introduction of immunohistochemistry, molecular cytogenetics and other molecular techniques
  - ❖ find a limited panel of antibodies suitable for our setting

## Conclusions

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4. The establishment of the Histopathology unit improved the quality of diagnosis and staging of pediatric patients with malignancies.
  - ❖ Reduced time to diagnosis
  - ❖ Reduced n. of non diagnostic specimens
  - ❖ Improvement of the differential diagnosis (use of the tru-cut biopsy)
  - ❖ Improved recruitment capacity by the clinical wards (early treatment, specific treatment ...)
  - ❖ Increased number of treated cases

# How to improve prognosis of the cancer

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## 1. Diagnostic Capacity

## 2. Standardize clinical practice

### ❖ Background

- ❖ Lymphoma treatment free for pediatric pt since '70
- ❖ Dedicate Unit in the pediatric department

### ❖ 2008

- ❖ Dedicate unit for cancer patients and dedicate senior clinician, dedicate nurse.
- ❖ Introduction of internal guidelines: treatment, supportive care, chemotherapeutic drugs.
- ❖ Internal "control": Electronic Database

## Burkitt's Lymphoma 2008-2009: Clinical Presentation

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<b>n.</b>	<b>158</b>	
<b>Age(range/median)</b>	<b>2-18y</b>	<b>7,8y</b>
<b>Sex (M:F/ratio)</b>	<b>88:81</b>	<b>1,1</b>
<b>HIV(tested/pos)</b>	<b>89</b>	<b>2</b>
<b>Stage C</b>	<b>111</b>	<b>70%</b>
<b>Stage D</b>	<b>36</b>	<b>23%</b>
<b>Stage B</b>	<b>11</b>	<b>7%</b>
<b>MEDIAN SIZE</b>	<b>7 CM</b>	
<b>DURATION</b>	<b>2 MONTHS</b>	
<b>B SYMPTOMS</b>	<b>67</b>	<b>42%</b>
<b>Abdomen</b>	<b>137</b>	<b>87%</b>
<b>Jaw</b>	<b>59</b>	<b>37%</b>
<b>CNS</b>	<b>34</b>	<b>22%</b>
<b>Lymphnodal</b>	<b>11</b>	<b>7%</b>
<b>Pleural</b>	<b>4</b>	<b>3%</b>

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## Staging

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### History and Physical Examination

Detailed clinical history (including demographic data)  
physical examination

**Measurement of palpable peripheral lymph nodes in centimeters**

### Blood Tests

Complete blood count (CBC)

Renal panel including serum creatinine and BUN (Blood Urea Nitrogen).

Hepatic panel including AST, ALT and Bilirubin if jaundice.

**HIV serostatus** (data available since 2009)

### Imaging Studies

Chest X-ray

Ultrasound of the abdomen (including liver and spleen) and pelvis

Other imaging studies as clinically indicated.

### Cerebral Spinal Fluid Examination

**It coincided with the administration of the first IT therapy and included cytology analysis. Since 2009 CSF cytology was monitored every course of chemotherapy.**

# Burkitt Lymphoma

## Signs and symptoms



## Clinical Classification

- A** → Unilateral involvement of the maxillary or mandible
- B** → Unilateral (both maxillary and mandible) or bilateral jaw's involvement
- C** → Abdominal (hepatosplenomegaly and abdominal/pelvic masses) or chest's involvement (mediastinum's enlargement or bloody pleural effusion)
- D** → Central nervous system (clinical: severe headache not responsive to analgesic drugs, ptosis/proptosis, paraplegia. Confirmed by cytology on the cerebro-spinal fluid which evidences atypical cells) or bone marrow (blasts  $\geq 5\%$  but  $< 25\%$  at the bone marrow aspirate) involvements .

## Burkitt's Lymphoma 2008-2009: Clinical Presentation

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# Burkitt Lymphoma

2008

1<sup>st</sup> line treatment: 6 courses of **COM**

1 course  
every 2 weeks

<b>Methotrexate</b> IT day 1, 2, 3* 10 mg 2-3 yrs 12 mg > 3 yrs	↓ ↓ ↓
<b>Cyclophosphamide</b> 1200 mg/sm IV <sup>^</sup> day 1	◇
<b>Vincristine</b> 1.4 mg/sm IV day 1	●
<b>Methotrexate 75 mg/sm IV day 1</b>	▨
<b>Day</b>	<b>1 2 3</b>
<sup>^</sup> NS or D5% 3000 ml/sm IV in 24 h Allopurinol 10 mg/Kg PO BD first courses to avoid lysis syndrome * <b>Citology of CSF at 1<sup>st</sup> LB of 1<sup>st</sup> course,</b> * <b>IT MTX: first 3 courses in CNS-, all 6 courses in CNS+ (stage D)</b>	

Start chemotherapy with a pt in fair general condition, afebrile, and if:

- PMN > 1.0 x 10<sup>9</sup>/L or PTL > 75 x 10<sup>9</sup>/L

**Pre-Phase: CTX 200mg/mq x 2-3dd + PND 1mg/kg x 5dd if unstable clinical conditions or bulky disease**

**Specific drug modification (VCR and MTX) if toxicities**

## 1<sup>st</sup> line therapy

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<b>BL: Registered Diagnosis 2008-2009</b>	<b>169</b>	
<b>Treated Pts</b>	<b>158</b>	
<b>Abandon/interrupted</b>	<b>27</b>	<b>16%</b>
<b>Evaluable for efficacy and toxicity</b>	<b>131</b>	<b>84%</b>
<b>CR</b>	<b>89</b>	<b>(68%)</b>
<b>Treatment failure</b>	<b>26</b>	<b>(20%)</b>
<b>non relapse mortality</b>	<b>16</b>	<b>(12%)</b>
<b>death acute phase</b>	<b>12</b>	<b>(9%)</b>
<b>lost to follow up</b>	<b>29</b>	<b>(25%)</b>
<b>median follow up(months)</b>	<b>12</b>	
<b>Relapse</b>	<b>21</b>	
<b>diagnosis to relapse(months)</b>	<b>5,2</b>	
<b>CNS relapse</b>	<b>13/21</b>	<b>(62% of rel.)</b>

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## Conclusions

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1. A chemotherapeutic regimen is feasible in our setting but
  - ❖ the treatment failure due to the abandonment (16%)
  - ❖ allocate resources for family support during treatment
2. COM is an effective regimen as first line chemotherapy for pBL patients (68% of response rate) but
  - ❖ the non relapse mortality is high (9% of early deaths) and advanced stages (C+D) 93% of our cases
  - ❖ *recruit the patients in earlier stages* → *find* common pathways of referral, increase awareness among clinicians, disseminate information about the availability of the treatment.

## Conclusions

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3. Relapse rate and CNS relapse is high (60% of rel)
  - ❖ Find prognostic score suitable for African BL
  
4. Design novel therapies adapted to local necessities and geographic requirements
  - ❖ Need of drugs active on the CNS (Ifosfamide, etoposide, MTX, AraC)

### Reinforce Network and collaborations

*international collaboration can overcome some of the resource limitations and provide training to the health providers.*

- ❖ **APOF** → introducing immunohistochemistry
- ❖ **INCTR** → Clinical practice, drugs, training

### Research

*clinical studies are feasible in developing countries and essential for the development of a relevant evidence base. They also contribute to the transfer of knowledge by providing a focus for training and education of staff and thus rapidly improve the quality of patient care.*

- ❖ **INCTR**
- ❖ **EMBLEM (NCI)**
- ❖ **University of Siena-Italy**

## Acknowledgements

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Fabio Ciceri MD



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**Prof Lorenzo Leoncini**

**EMBLEM TEAM- Sam M. Mbulaiteye**

MD

**INCTR**

**Prof Ian Magrath**



Thank You!!





## 2<sup>nd</sup> Line

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<b>Eligible for second line(n.)</b>	<b>47</b>
<b>Abandon/interrupted</b>	<b>12(21%)</b>
<b>CR</b>	<b>17</b>
<b>Treatment failure</b>	<b>18</b>
<b>Non relapse mortality</b>	<b>0</b>

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