

# **Pediatric Non Hodgkin's Lymphoma**

## **Local approach: Global impact**

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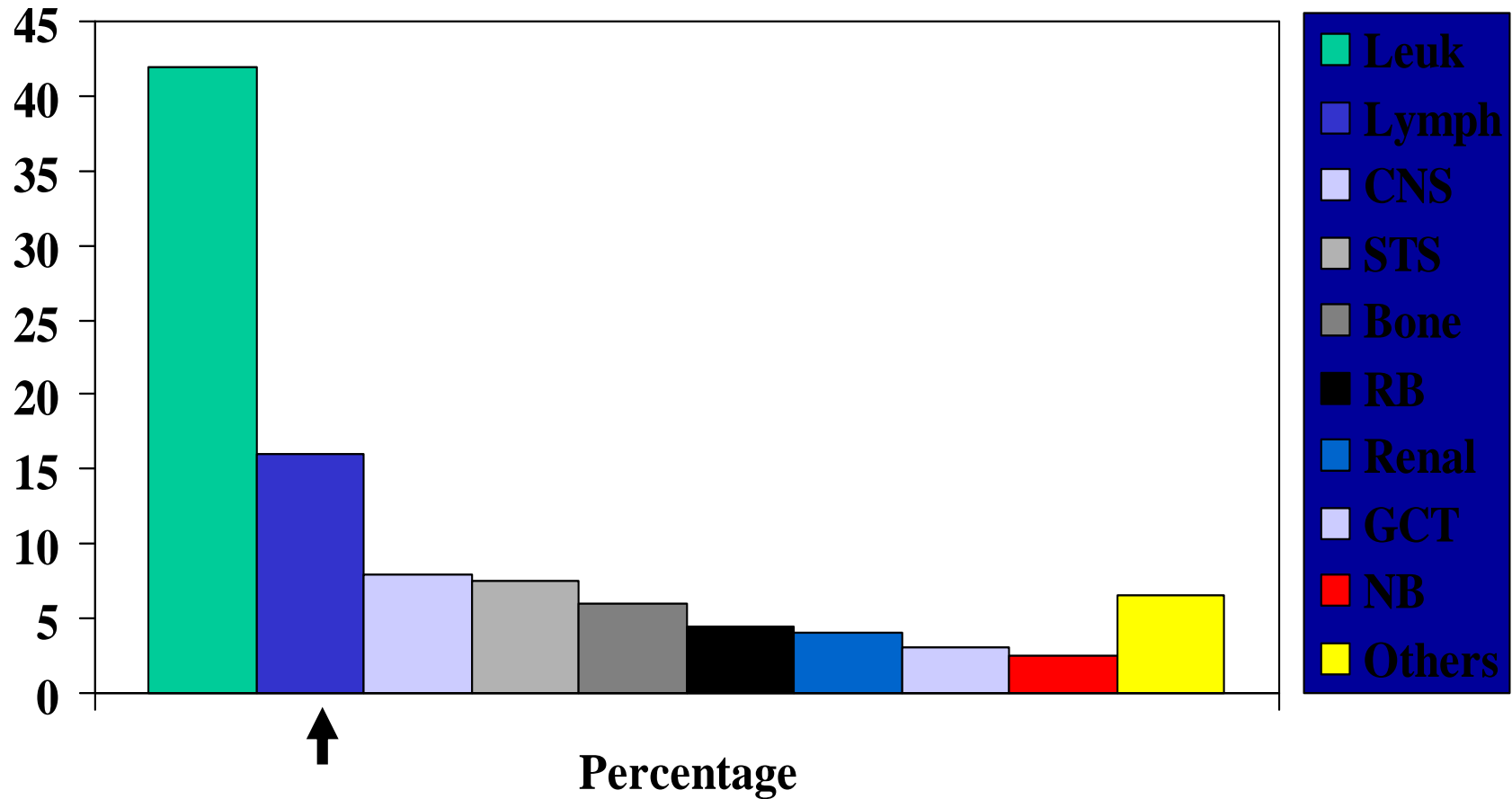
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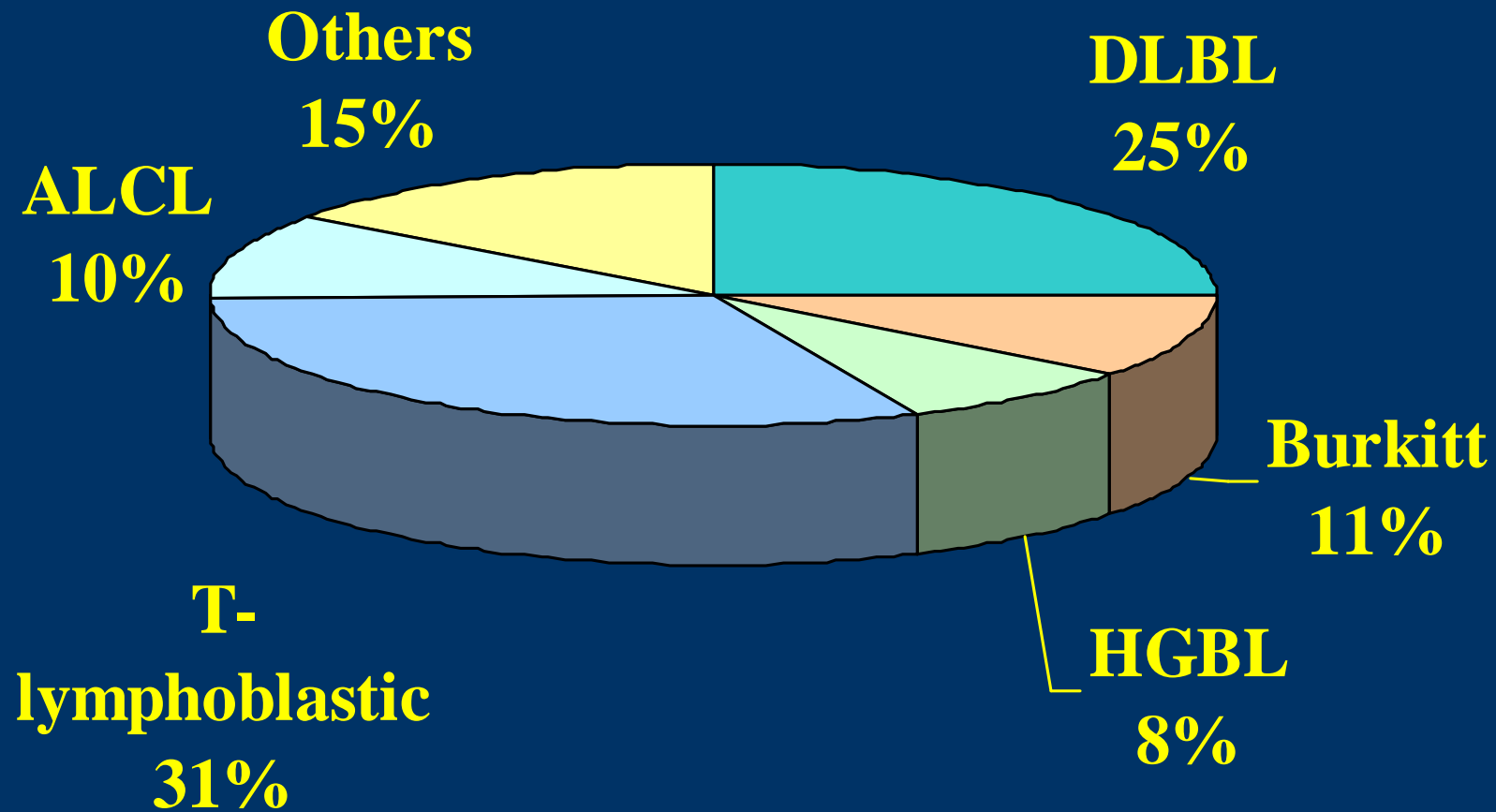


# TMH: Pediatric Cancer 800 to 1000 New Cases / Year



# The Indian Lymphoma Registry Data

## Pediatric NHL in <20 years in India



A Study of the Distribution of 289 Non Hodgkins Lymphomas using the WHO Classification among Children and Adolescents in India.

Srinivas et al, Med Pediatr Oncol 2002

# Pediatric NHL: Geographic Differences

<u>Type</u>	<u>Europe &amp; USA (%)</u>	<u>India (%)</u>
LL	33	32
BL & BLL	50	23
LCL:	15	33
ALCL	07	11
LBCL	08	22
Others	02	12

## Non-Hodgkin's Lymphomas in Children, Clinical Histological and Treatment Analysis

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### SUMMARY

One hundred and eighty one cases of non-Hodgkin's lymphomas in children between 1½ to 20 years of age presenting at Tata Memorial Hospital, Bombay from 1976 to 1982 were studied. Undifferentiated lymphoma (Burkitt's and non-Burkitt's) was the commonest subtype (40.9%) followed by lymphoblastic lymphoma (25.4%) and diffuse histiocytic (11.1%). Commonest site of presentation was abdominal (37.3%) followed by mediastinal (13.6%). Majority of patients presented in stage III & IV (71.6%) at diagnosis. Of the 97 patients who received adequate treatment in the form of COP or CHOP chemotherapy, complete remission was obtained in 68.8% of COP and 87.9% of CHOP group. The five year acturial survival in adequately treated patients was 39 per cent. The five year survival in undifferentiated non-Burkitt's was worst (9.5%). Stage I & II patients fared better than stage III & IV patients. The presents study emphasises the need for aggressive approach to paediatric NHL.

NON-HODGKINS LYMPHOMA IN CHILDREN 1976-82 T.M.H  
 ACTURIAL SURVIVAL IN RELATION TO STAGE  
 AND CHEMOTHERAPY

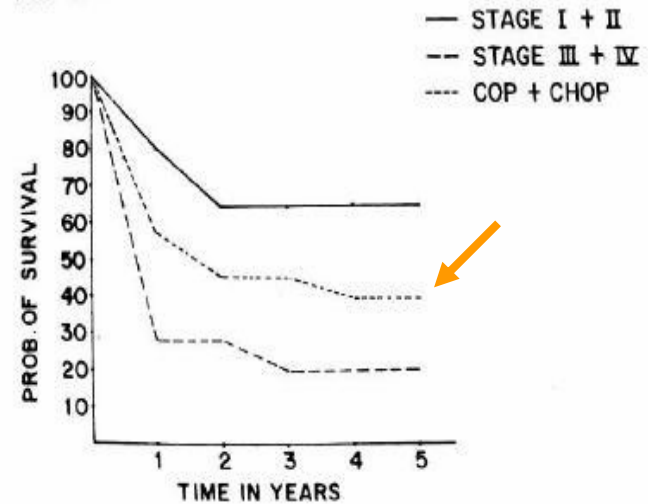


Fig. 1

NON-HODGKINS LYMPHOMA IN CHILDREN 1976-82 T.M.H  
 ACTURIAL SURVIVAL IN RELATION TO HISTOLOGY

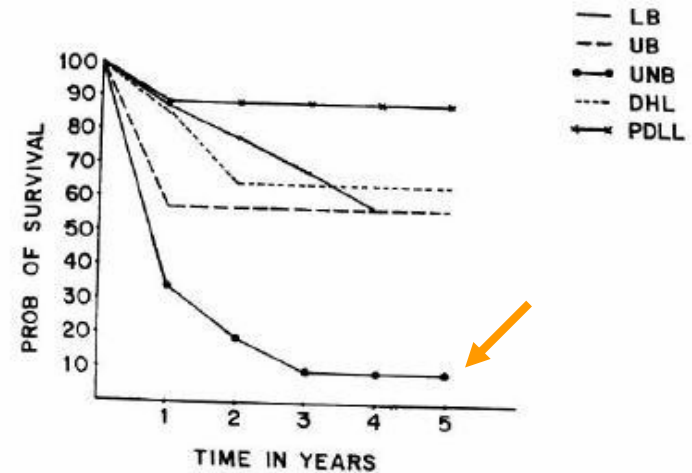
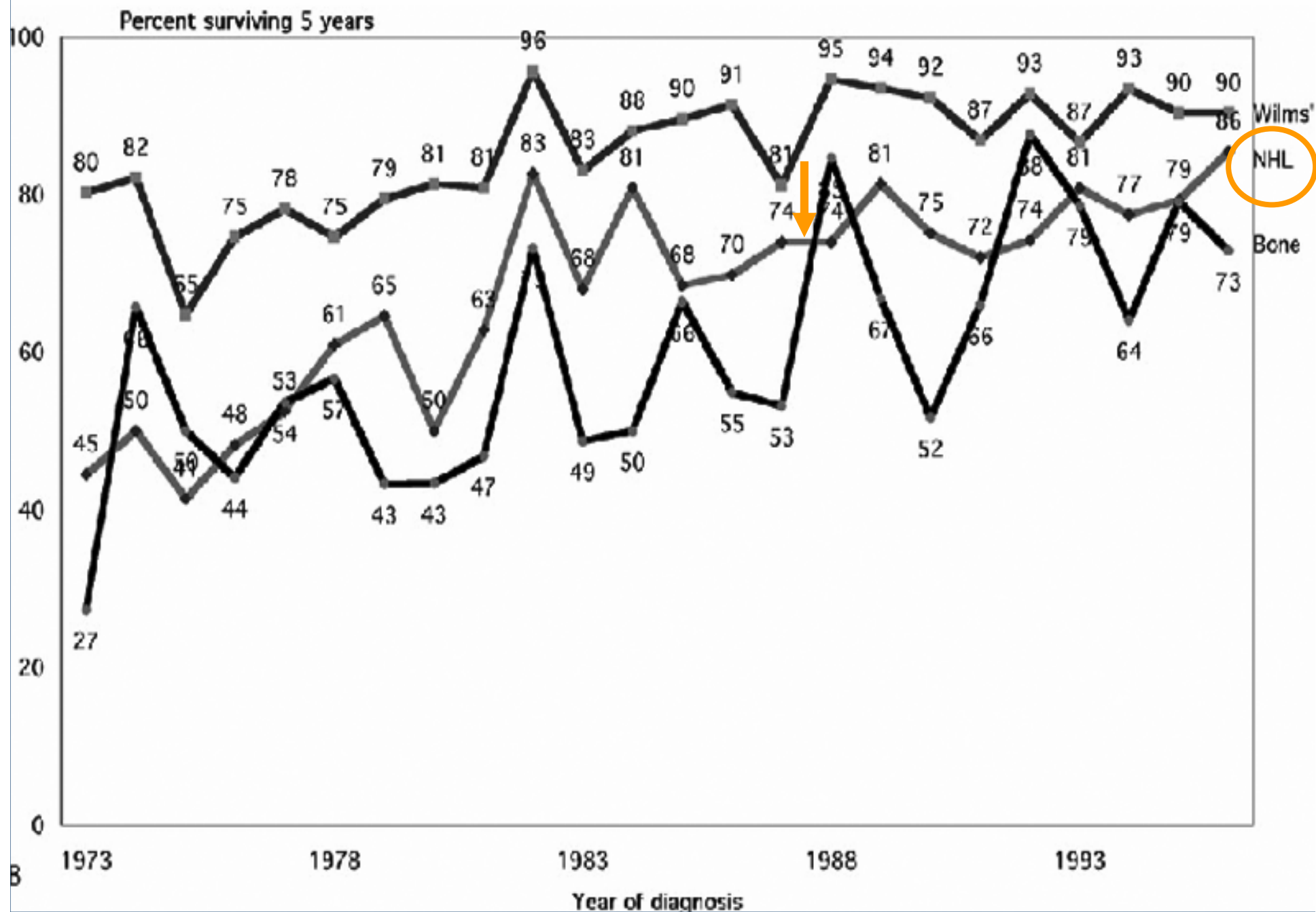


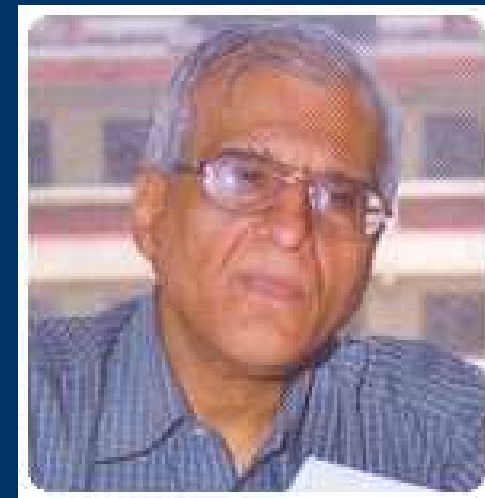
Fig. 2



## Need for an indigenous protocol

- Good Efficacy
- Low-cost
- Less toxic
- No high dose methotrexate
- Minimal supportive care requirements
- Could be given on outpatient basis

# Genesis of Protocol MCP-842



# MCP - 842 PROTOCOL

## Regimen A:

VCR 1.4 mg/m<sup>2</sup>

CTX 800 mg/m<sup>2</sup>- d 1

200 mg /m<sup>2</sup> – d 2-4

ADR 20mg /m<sup>2</sup>

ARA-C 500 mg /m<sup>2</sup>

IT-ARAC 70 mg

IT-MTX 12 mg

## Regimen B:

VCR 1.4 mg/m<sup>2</sup>

IFOS/MSNA 1200 mg/m<sup>2</sup>

ETOP 60 mg/m<sup>2</sup>

MTX 15 mg/m<sup>2</sup>

IT-ARA-C70 mg

IT-MTX 12 mg

Week 1



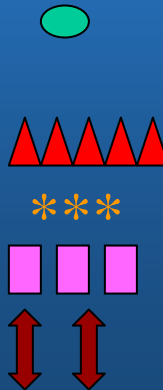
Week 2



Week 3



Week 1



Week 2



Week 3



## Original article

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### **Preliminary report of an intensified, short duration chemotherapy protocol for the treatment of pediatric non-Hodgkin's lymphoma in India**

S. Advani,<sup>1</sup> S. Pai,<sup>1</sup> M. Adde,<sup>2</sup> S. Vaidya,<sup>1</sup> T. Vats,<sup>3</sup> K. Naresh,<sup>1</sup> P. A. Kurkure,<sup>1</sup> C. N. Nair,<sup>1</sup>  
D. Venzon<sup>2</sup> & I. Magrath<sup>2</sup>

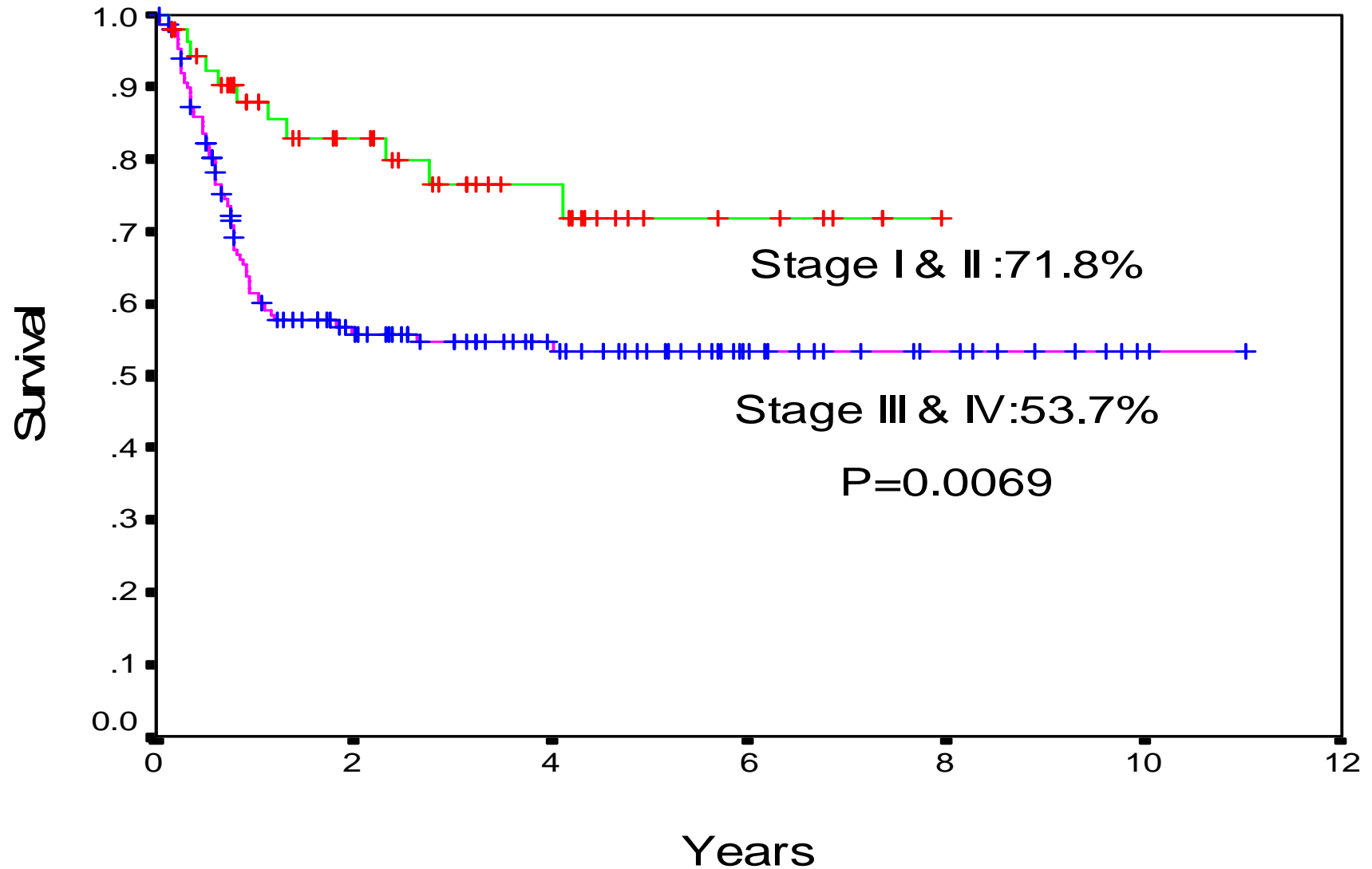
<sup>1</sup>Tata Memorial Hospital, Bombay, India; <sup>2</sup>National Cancer Institute, Bethesda, MD, <sup>3</sup>Texas Tech University, Amarillo, TX, USA

# Advantages of MCP-842

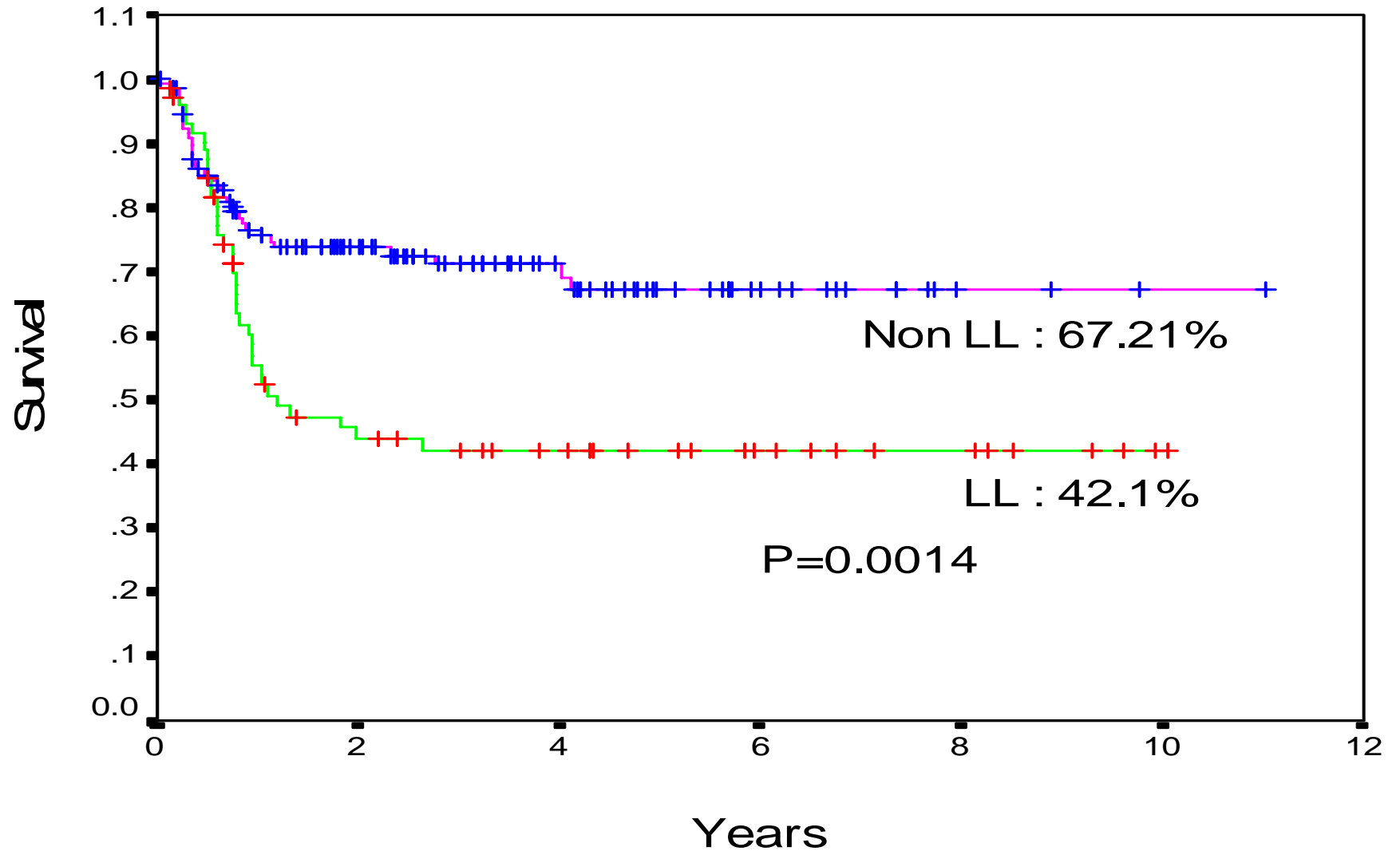
- Same Protocol for all subsets.
- Excellent tolerability: Rx given on out-pt basis
- Minimal supportive care requirements
- No need for total parental nutrition
- Minimal transfusion, growth factor & IV antibiotic requirements.
- No RT in the protocol

**FEASIBLE IN DEVELOPING COUNTRIES WITH LIMITED RESOURCES**

# MCP 842 Protocol: Survival (1987 – 2001)



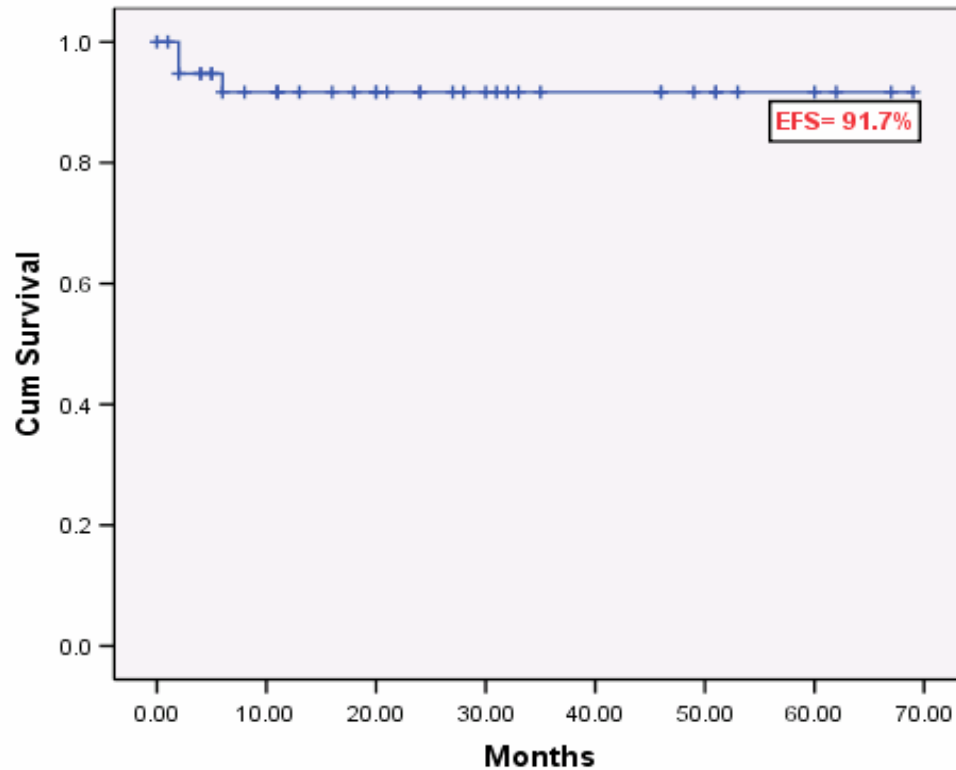
# MCP 842 Protocol: Survival (1987 – 2001)



## MCP 842 : Modifications for LL

- Jan 2002: 4 Maintenance cycles (12 months) of ALL Rx added.
- EFS improved to 54% (13 Pts).
- More than 50% relapses observed before starting Maintenance!
- June 2003: Patients with LL Stage I to III treated with Modified BFM 90 Protocol (HD MTX: 3gm/m<sup>2</sup>). *Reiter A et al. Blood 2000; 95:416-21*  
Stage IV Rxed as ALL on MCP-841 protocol

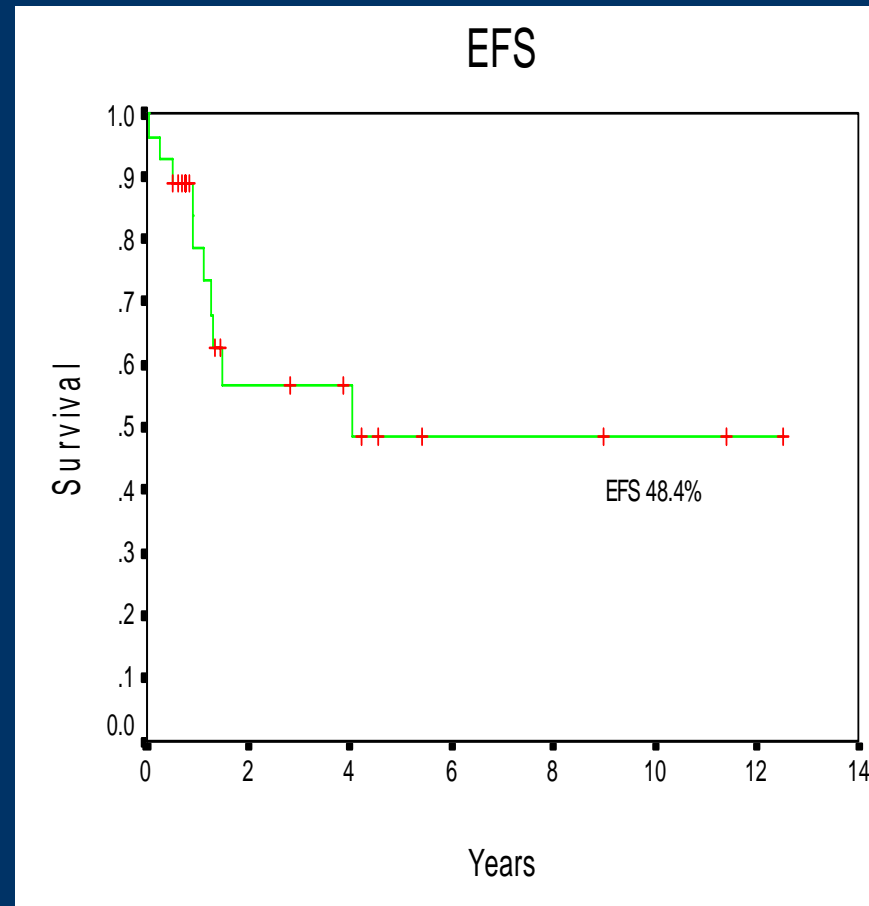
# LL: Modified BFM-90 (2003-2008) (N-40)



**3 Toxic Deaths**  
**No relapses so far!**

**ANC > 1000; MTX 3 G/m<sup>2</sup>**

# MCP-842 Protocol: Efficacy in ALCL



## **MCP 842: Modifications for ALCL**

- Most relapses on standard MCP-842 salvaged with Vinblastine based therapy. So Vinblastine was added from 2004.

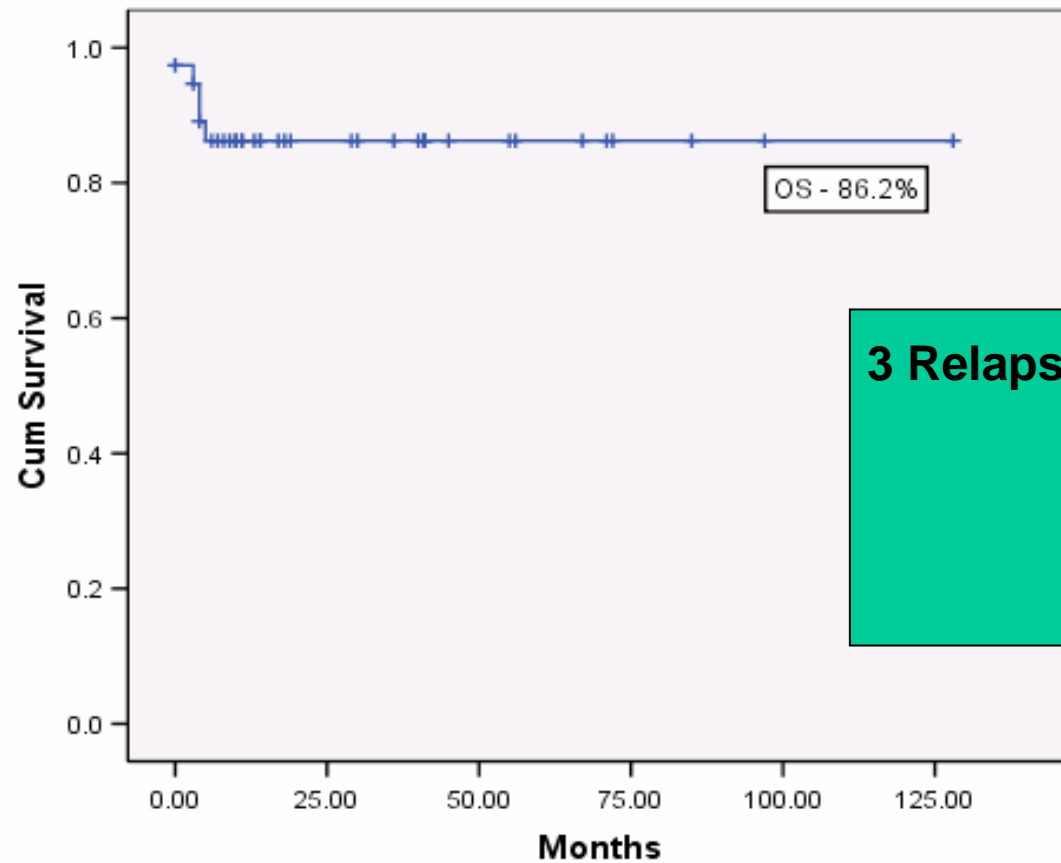
**VCR replaced with Vinblastine 6 mg/m<sup>2</sup> in MCP-842.**

- Most relapses observed after completion of MCP 842. So maintenance therapy added from 2004.

**ALL like 6MP + Mtx added as maintenance:**

**6 months for Stg I & II; 12 months for Stg III & IV**

# ALCL: Modified MCP-842 (1997-2008) (N-38)

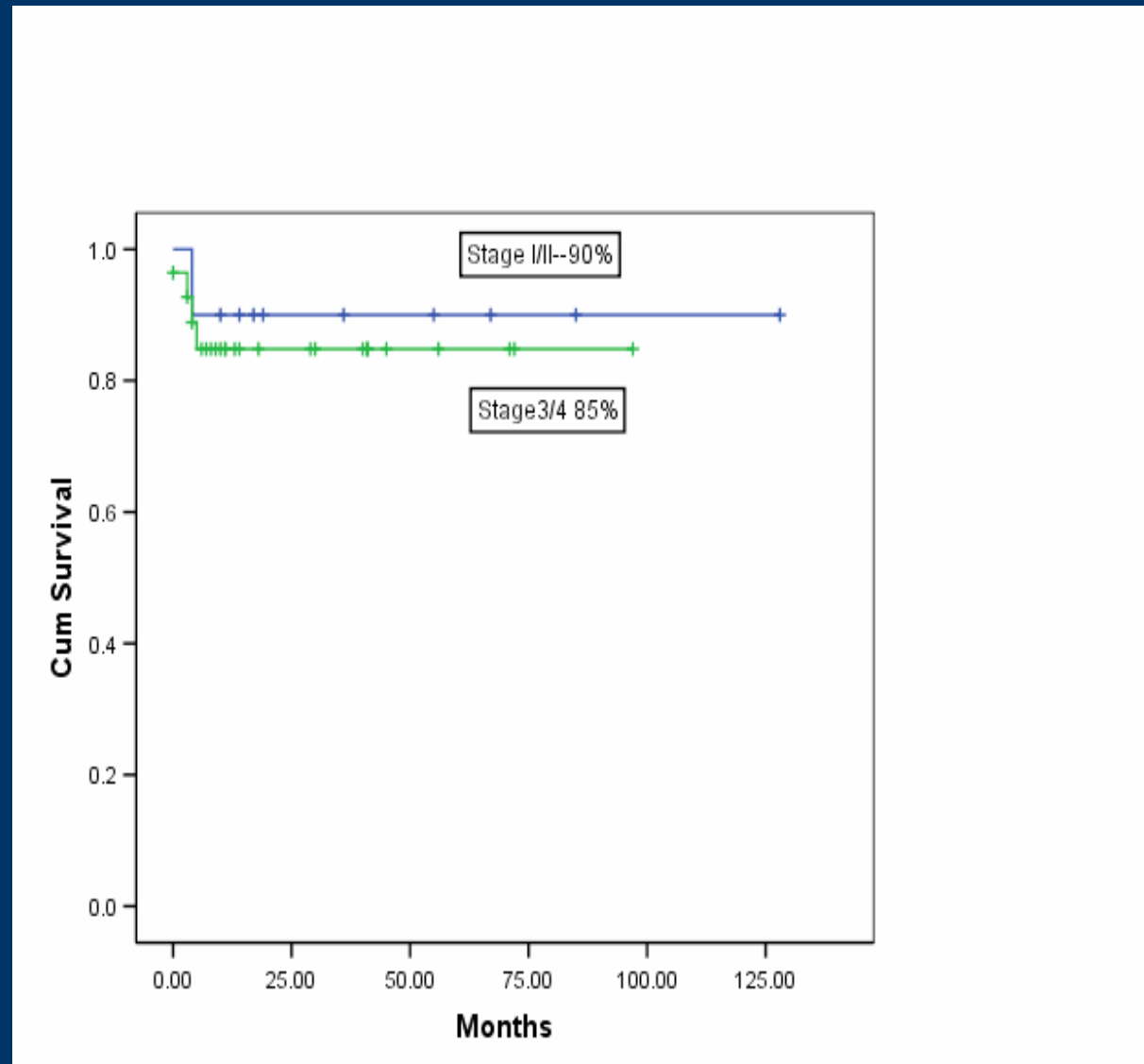


**3 Relapses from Pre-Mod. era salvaged**

**3 toxic deaths**

**No relapses so far**

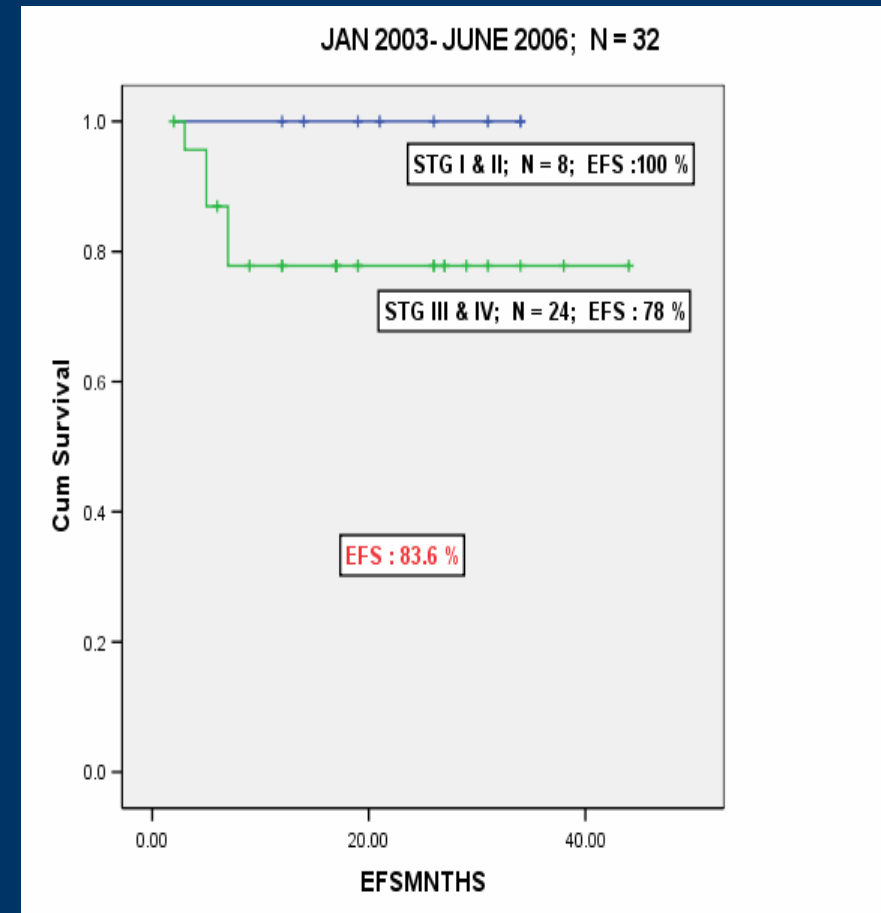
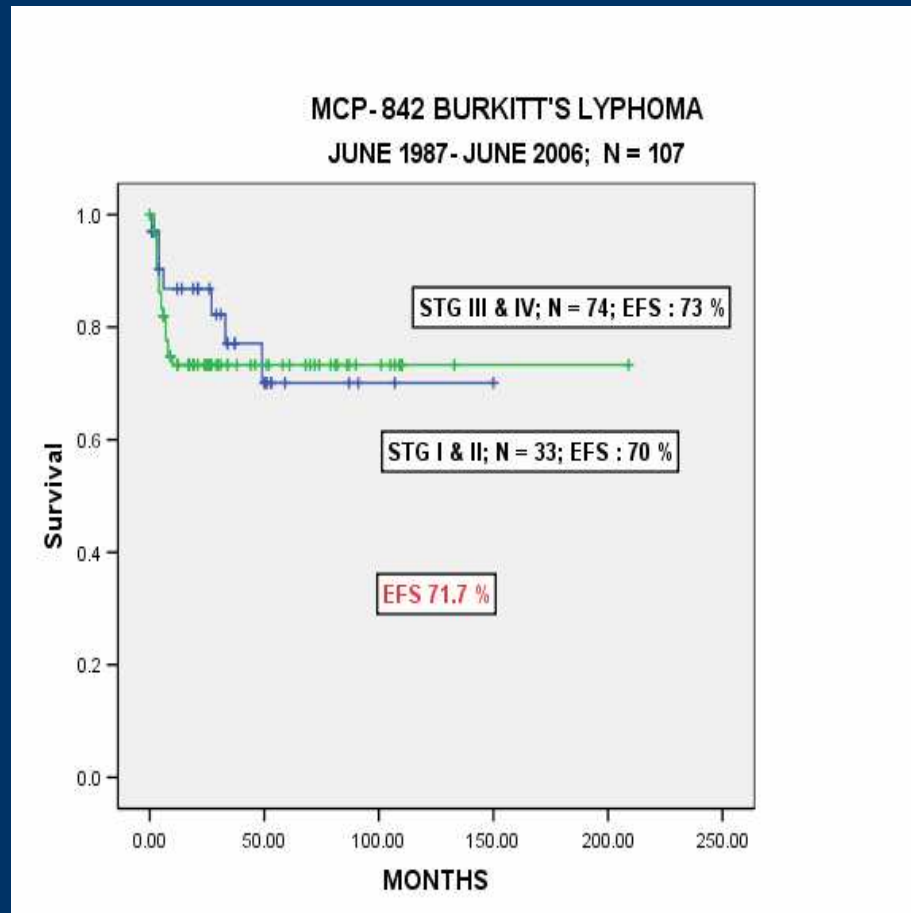
# ALCL: Modified MCP-842 (1997-2008) (N-38)



# **MCP 842 :Modifications for B-NHL**

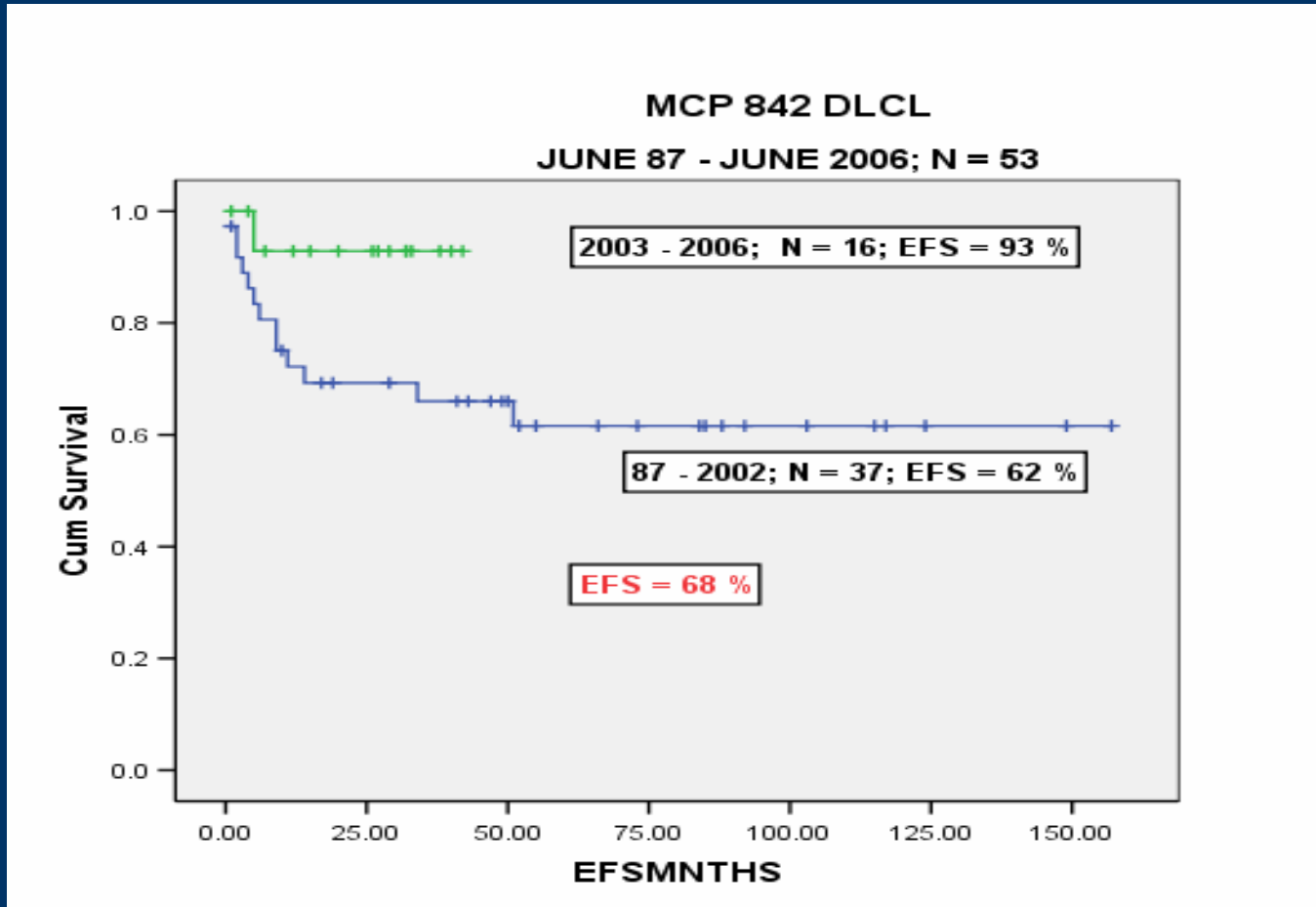
- **COP Window for bulky disease or unstable patients**
- **Aggressive upfront therapy & avoiding delays**
- **Improved supportive care including use of rasburicase.**
- **RT to Bones in Pts. with DLBCL & bone involvement.**
- **All pts. received 8 cycles of CT.**

# Modified MCP-842: Burkitt's Lymphoma



*Arora B, Banavali SD et al short duration intensive chemotherapy protocol for treatment of small non-cleaved cell lymphoma (SNCL) in children and young adults. Pediatr Blood Cancer , 2005; 45:533*

# Modified MCP-842 for DLBL



*Arora B, Banavali SD et al. Clinical presentation & outcome of children with Diffuse large B-cell lymphoma treated with a uniform short duration intensive protocol in India. Pediatr Blood Cancer , 2007; 49:524*

# Thus..

- Start from your failures! First analyze where you have failed.
- Small changes done at the right place can make differences!
- One does not always have to become more aggressive to improve results!

## Thus..

- Modified MCP-842 is highly efficacious for B-NHL and ALCL in children
- Safe, outpatient therapy
- Minimal supportive care
- Cost effective
- Model protocol for a developing country

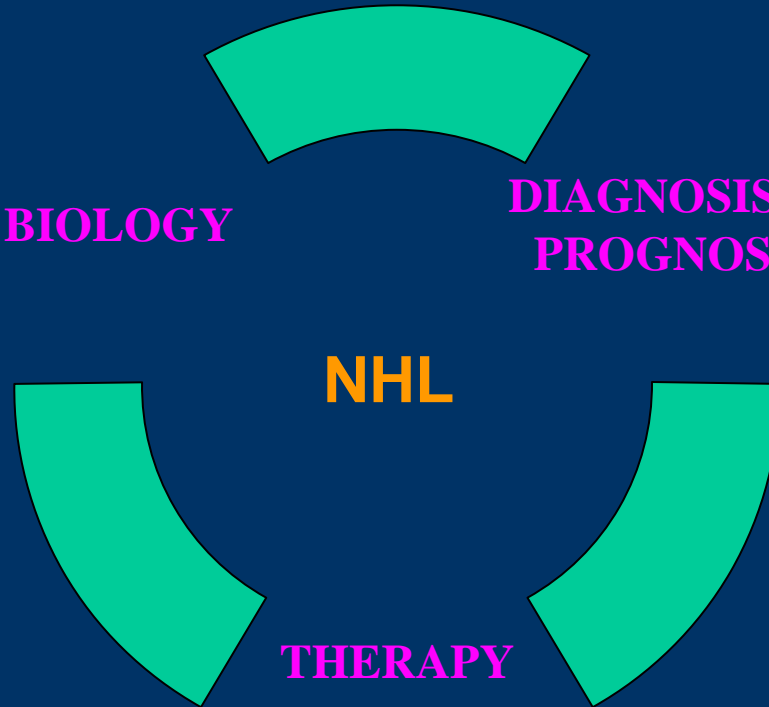
# Future Focus

**BIOLOGY**

**DIAGNOSIS &  
PROGNOSIS**

**NHL**

**THERAPY**



# Biology

- **Identify extremely low risk T-LL requiring low intensity therapy**
- **Elucidate the basis of exquisite sensitivity of ALCL to vinblastine**
- **Molecular genetics and expression profile of T-LL and ALCL & Correlation with immunophenotype and prognosis**

# Diagnosis and Prognosis

- Identify high risk B-NHL group based on early clinico-metabolic response
- Correlation of early clinical (day-7) response and PET response

# Therapy

- Evaluation of augmented MCP-842 protocol incorporating Rituximab and intermediate dose methotrexate for high risk B-NHL



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Thank You