

REPORT ON THE EDUCATION AND RESEARCH OF LYMPHOMA IN CHINA



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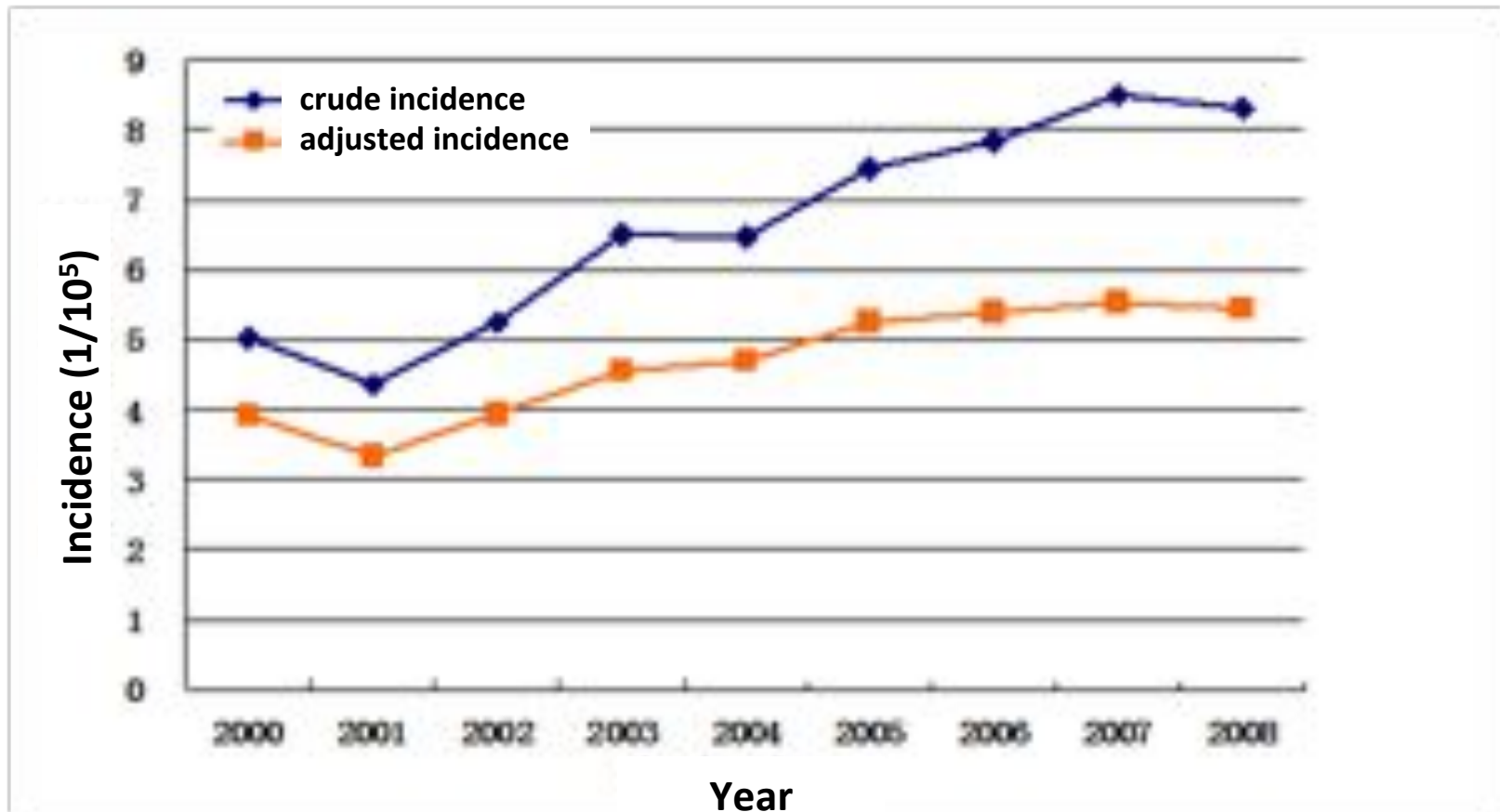
Overview

- ❑ **Education Activity of Chinese Society of Lymphoma, CACA**
- ❑ Frequencies of Lymphoma Subtypes & NK/T Cell Lymphoma Research in China



Epidemiology of lymphoma in China

Incidence trend of malignant lymphoma from 1998 to 2008
6.4/100,000 in 1998 and 10-11/100,000



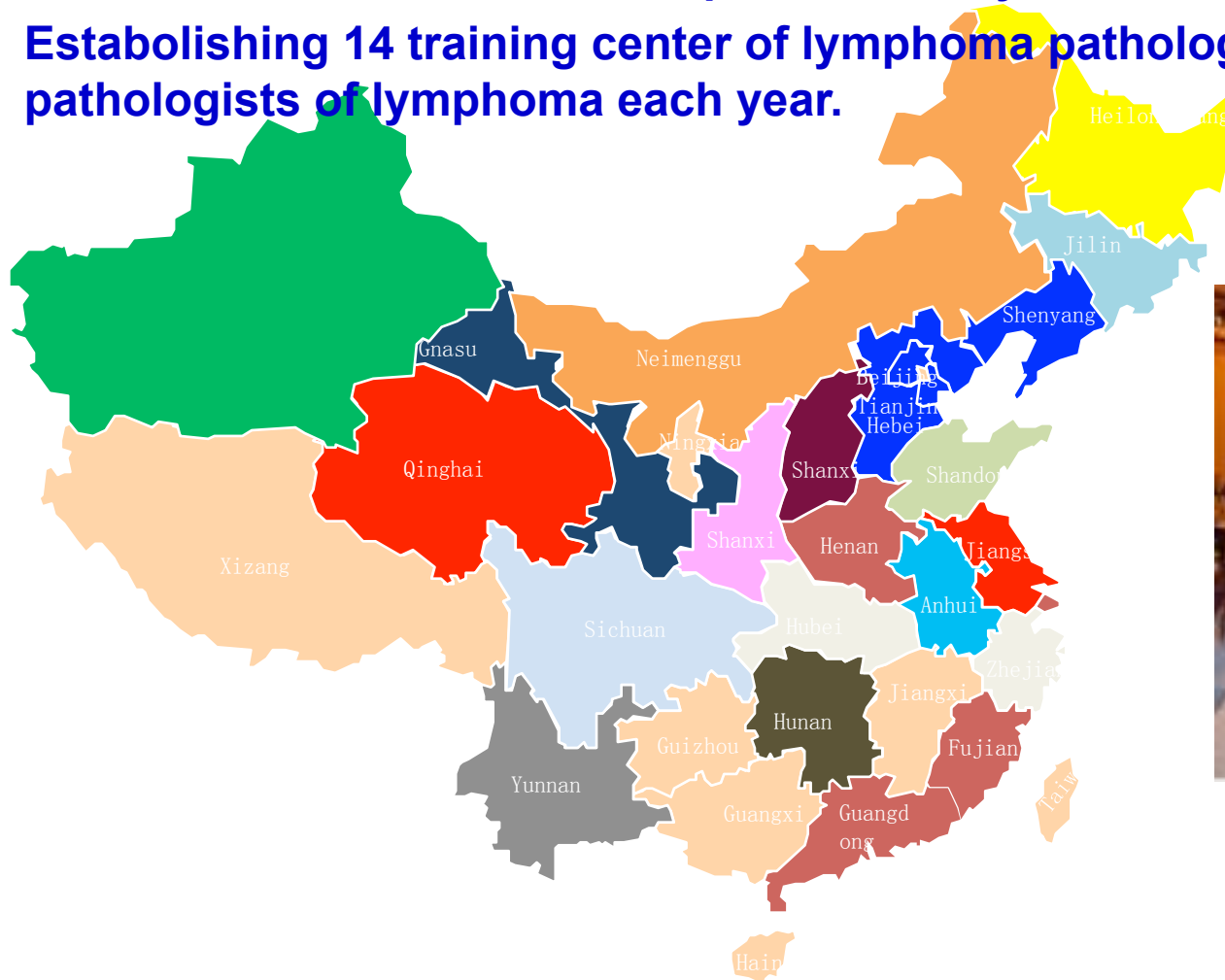
The Mission of Committee of Malignant Lymphoma, Chinese Anti-cancer Association



The Further Education of the Medical Oncologist In China

The interpretation of the Chinese Lymphoma Guideline was carried out in more than 25 cities in China from Sept 2011 to May 2012

Establishing 14 training center of lymphoma pathology, training more than 100 pathologists of lymphoma each year.



Chinese collaborative group of pathology in malignant lymphoma

- **Members of the Chinese collaborative group visit the departments of pathology in more than 80 hospitals with academic exchanges and guidance**



Education and Care of Patients with Lymphoma

Homeland-care for lymphoma patients 2011



Recovery Classroom

- ❑ Recovery Classroom:
 - Teaching the knowledge of lymphoma
 - Doctor-patient communication
 - Good platform for patients' communication
- ❑ Recovery Classroom was held more than 70 times in 37 hospitals



Website of Homeland-care for lymphoma patients

Website is easy to use, ie:

- About me

康复课堂公告



福建省肿瘤医院将于10月19日举办淋 **淋巴瘤**

苏州大学附属第一人民医院将于1 **淋巴瘤**

江西省肿瘤医院将于9月30日举办淋

武汉同济医院将于9月29日举办淋

济南齐鲁医院将于9月28日举办淋



中国淋巴瘤患者关爱家园

服务热线: 8008208657 / 4008208657

淋巴瘤知识

淋巴瘤可以治愈吗

家园介绍

专家推荐

康复园地

康复课堂公告



康复课堂公告

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山西省肿瘤医院将于8月22日举办淋巴瘤患者康复课堂

各位淋巴瘤患者及家属:

您好!

近年来随着社会的发展和居民生活方式的改变,以及大众健康教育的普及,越来越多的患者及家属希望得到淋巴瘤早期发现和有效治疗

> 淋巴瘤可以治愈吗



> 专家推荐

Lymphoma Hotline



Transfer
standardized
treatment
&
Recovery
Classroom, Free
Clinic Notice,
Web Caution

The Mission of Committee of Malignant Lymphoma, Chinese Anti-cancer Association



Overview

- Education Activity of Chinese Society of Lymphoma, CACA
- **Frequencies of Lymphoma Subtypes & NK/T Cell Lymphoma Research in China**

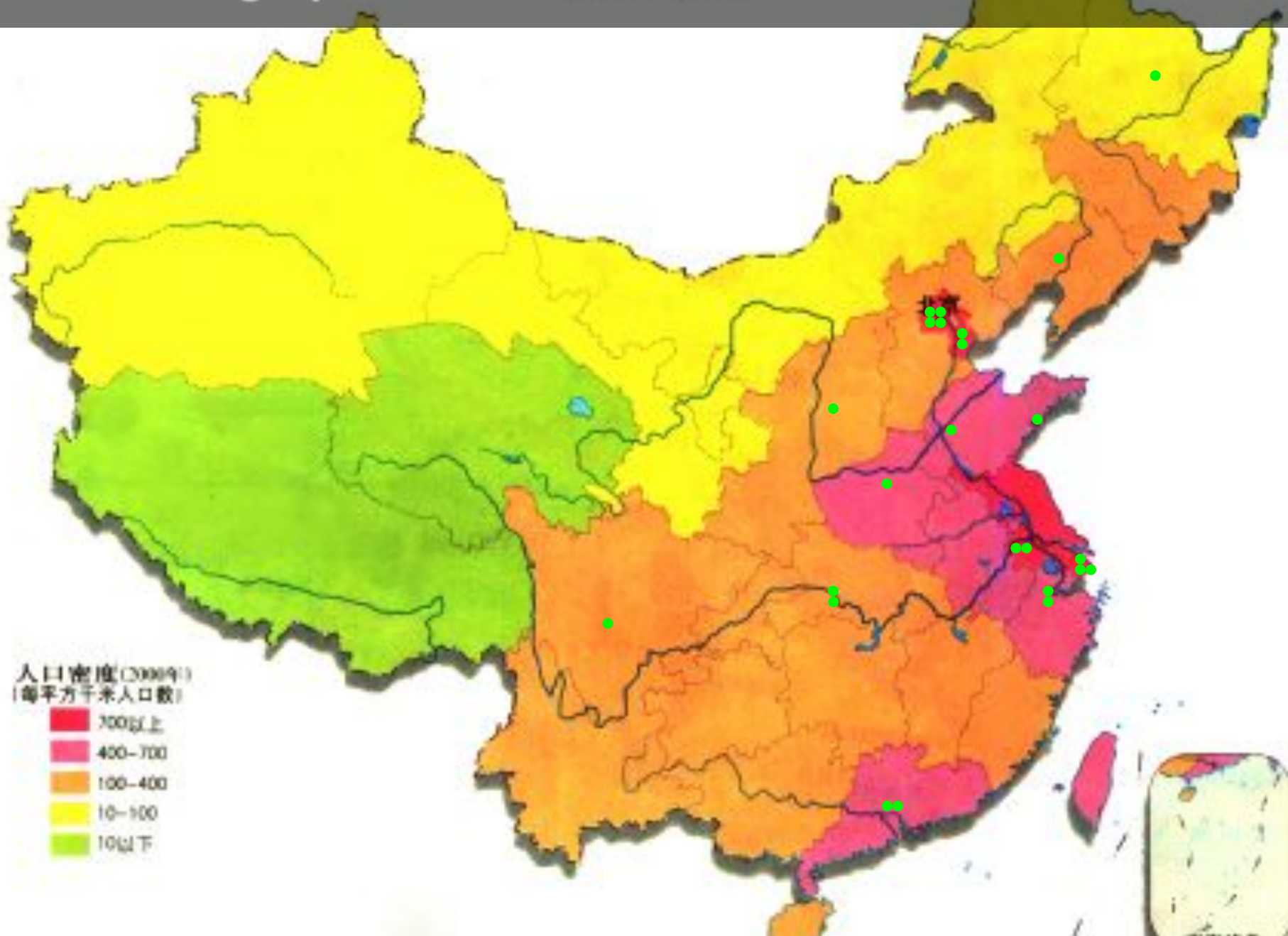


The Relative Frequencies of Lymphoma Subtypes in China: A Nationwide Study of **10002 Cases** by the Chinese Lymphoma Study Group (CLSG)

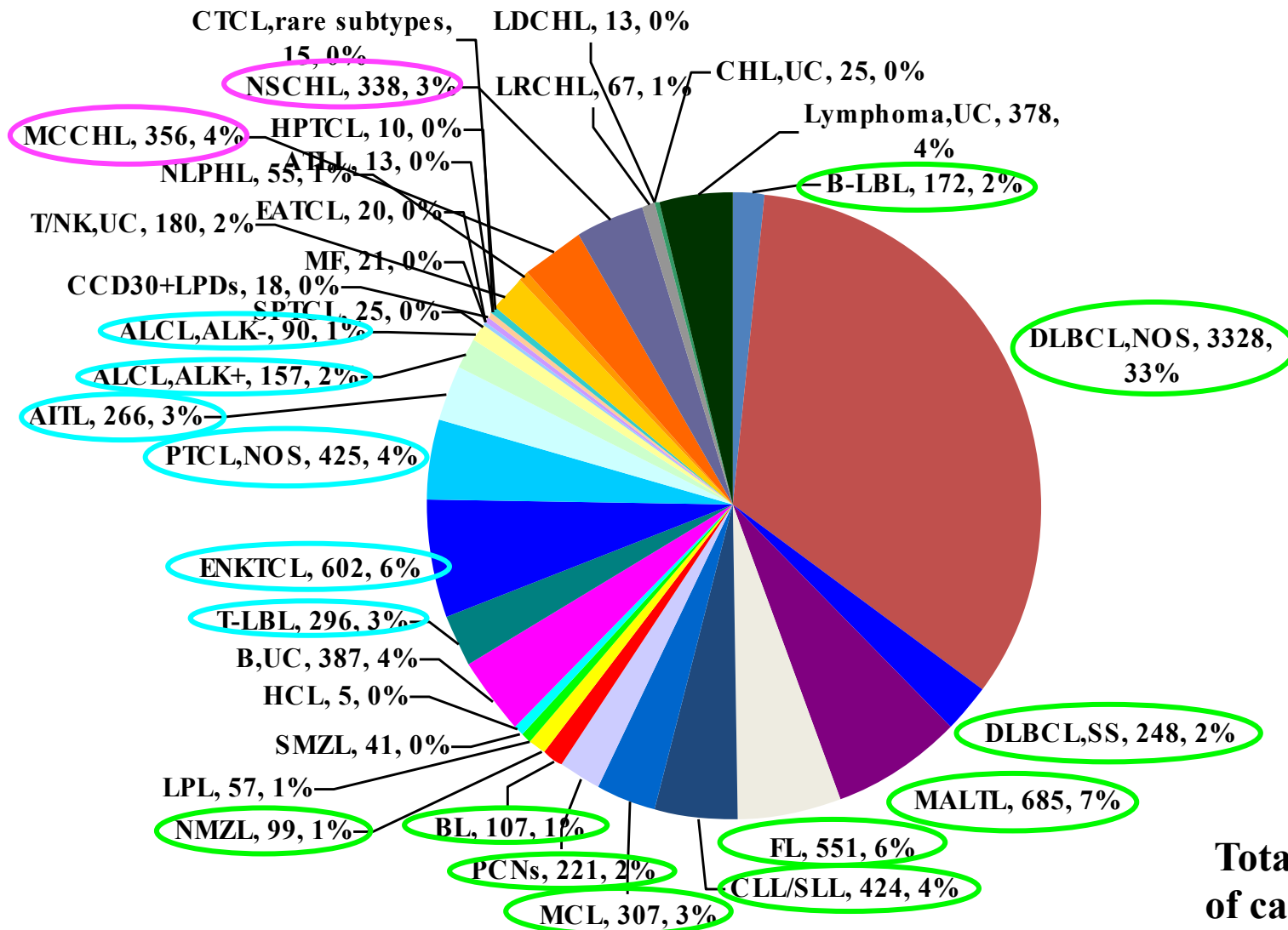


Geographic distribution of the 24 institutes

中国省级行政单位的人口密度
1:500,000



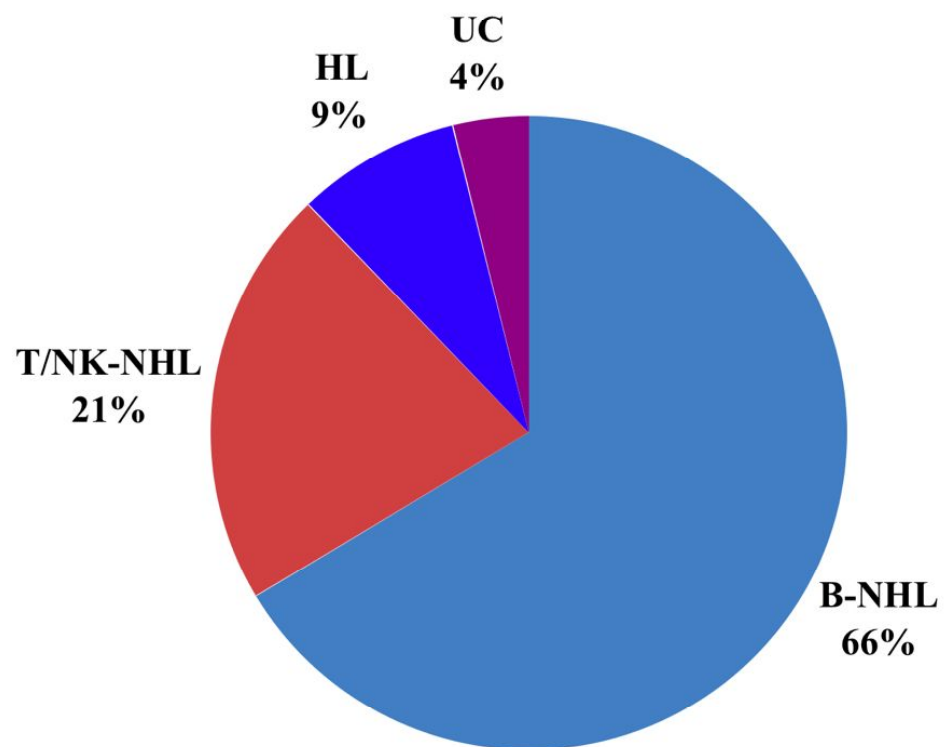
The relative frequencies of NHL and HL subtypes



Total number
of cases:10,002

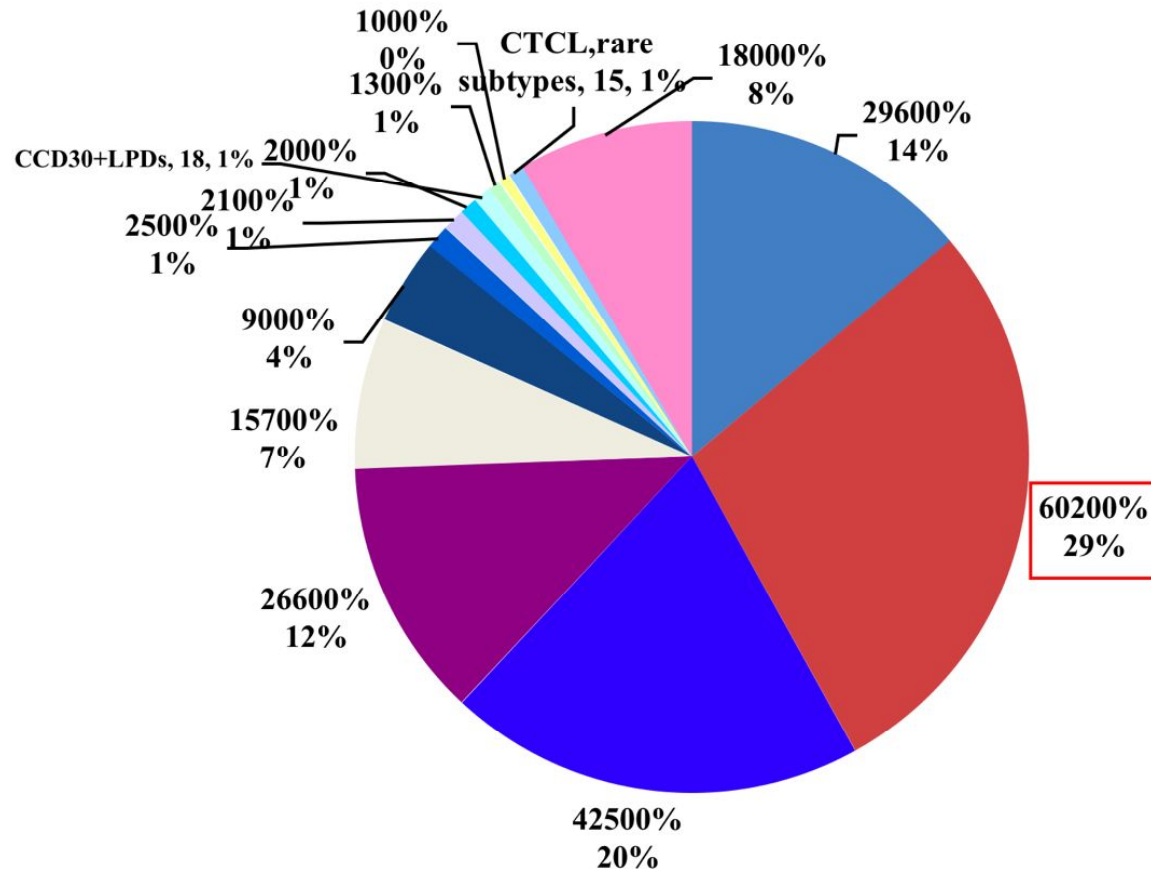
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The relative frequencies of HL and NHLs



**Total number
of cases : 10,002**

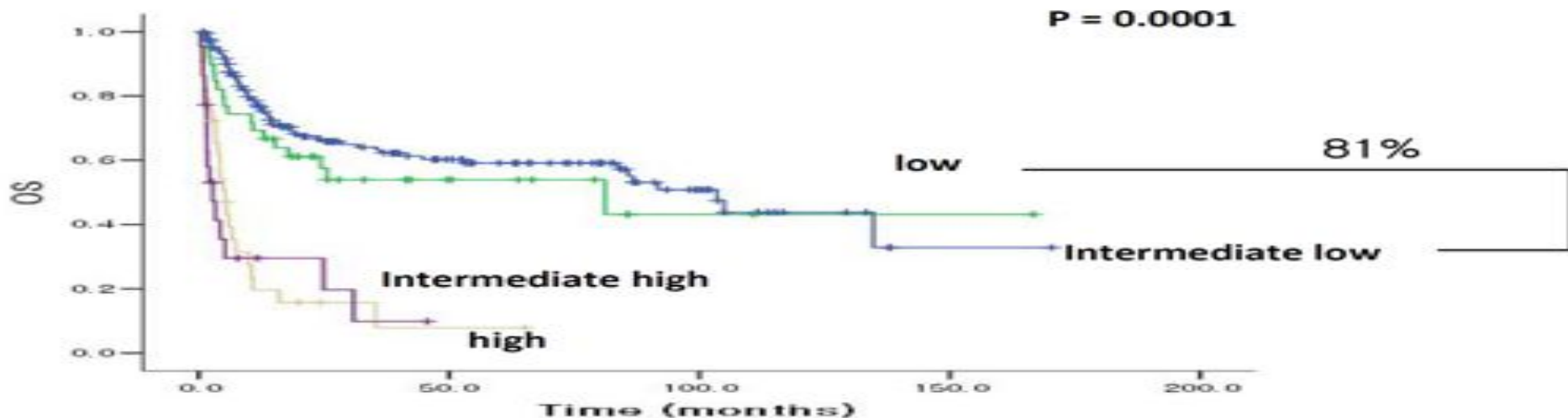
The relative frequencies of T/NK-NHL subtypes



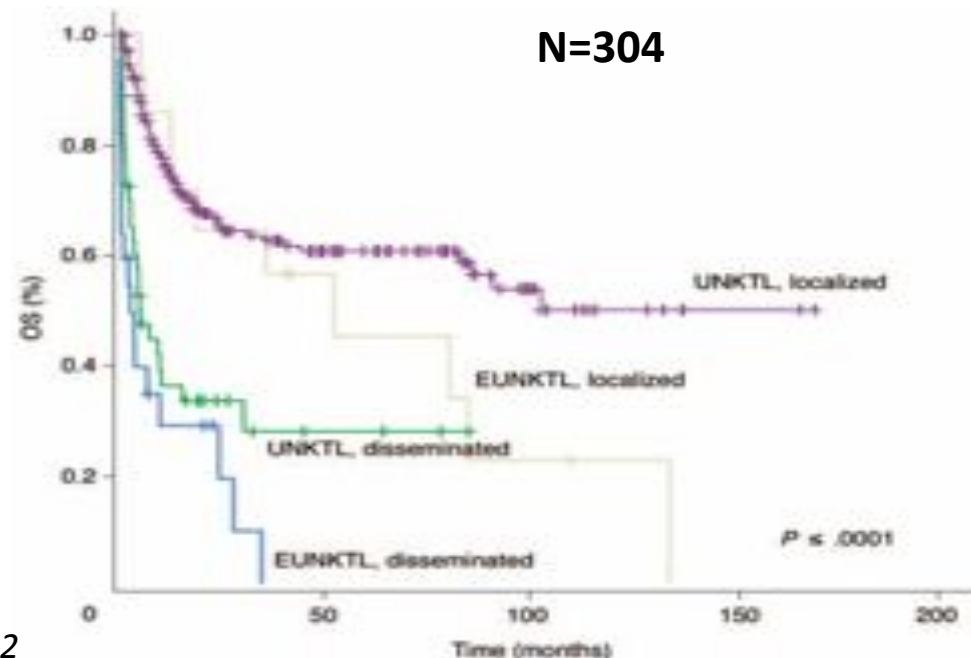
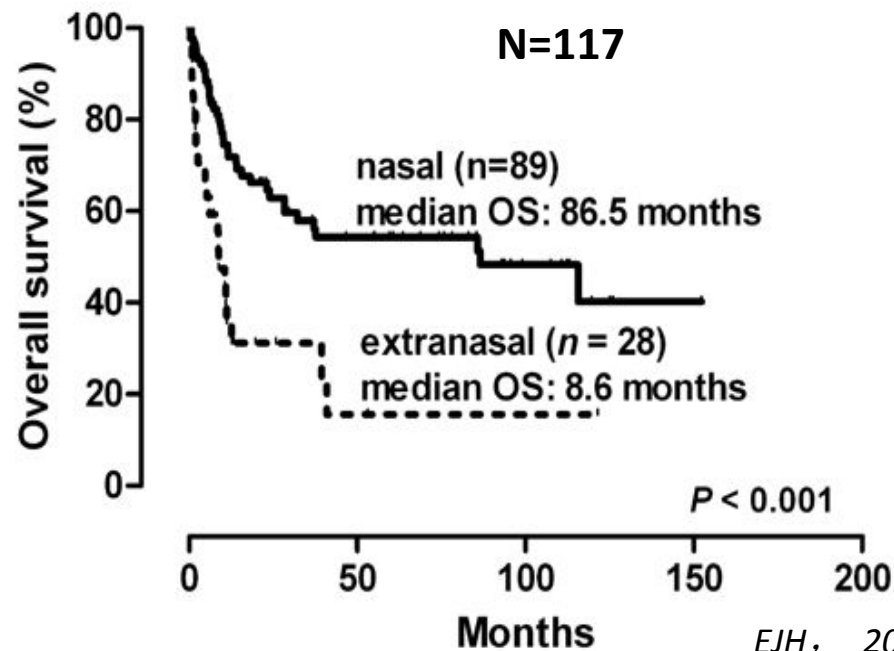
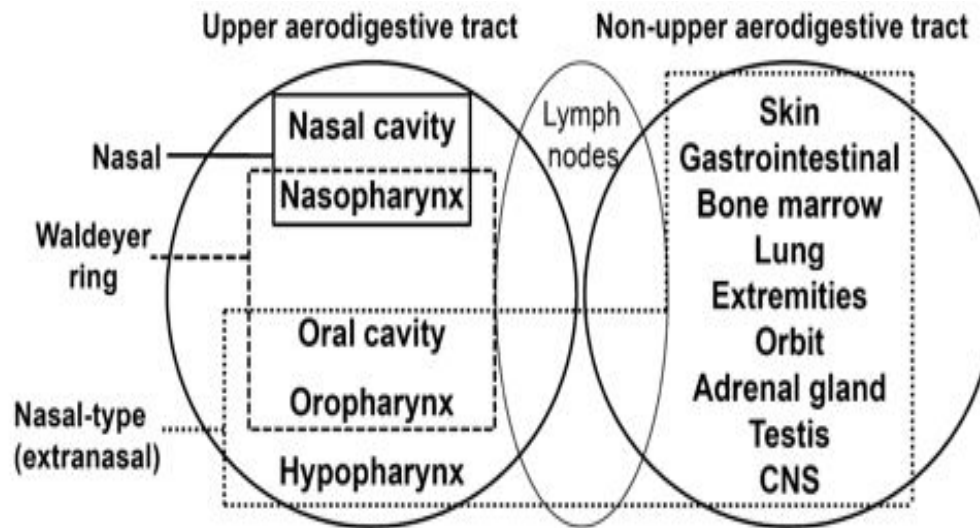
**Total number
of cases: 2,138**

Clinical features of NK/T cell lymphoma

- ❑ Ann Arbor staging I/II > 70%
- ❑ CHOP often resistance
- ❑ Media OS < 1 year for extra-nasal NK/T cell lymphoma
- ❑ EBV infection, EBER(+) 21-92%



NK/T cell lymphoma: different locations, different outcomes



Chemotherapy alone in NK/T cell lymphoma

Author	Pub. Time	n	Lesions	Stage	Chemotherapy Regimen	Effects (%)			
						CR	PR	SD	PD
Cheung	2002	61	Nasal	I-II	ProMACE-Cytabine, CHOP	49			51
Ribrag	2001	12	Nasal	I-II	CHOP, CHOP-like	25	42	0	33
Kim GE	2001	39	Nasal	I-II	CHOP, BACOP	6	46		49
Kim WS	2001	15	Upper AD tracts	I-II	CHOP	40	20		40
Kim BS	2003	69	Upper AD tracts	I-IV	CHOP, COPBLAM-V	35.6	10	24	30.5
Li CC	2004	18	Nasal	I-IV	CHOP	50			
Kim K	2005	16	Upper AD tracts	I-II	CHOP, COPBLAM-V	38	19	0	44
Kim SJ	2006	43	Upper AD tracts	I-II	CHOP	44	23		33
Pan ZH	2006	34	Upper AD tracts	I-IV	CHOP, EPOCH	44	26	15	16
He YF	2006	27	Upper AD tracts	I-II	CHOP, EPOCH	30	18	22	30
Li YX	2006	40	Nasal	I-II	CHOP, BACOP	20	40	18	22
Bossard	2007	48	Nasal	I-IV	CHOP, ACVBP, COPADM	60	0	0	50
Guo	2008	69	Nasal	I-IV	CHOP	49	10	20	20

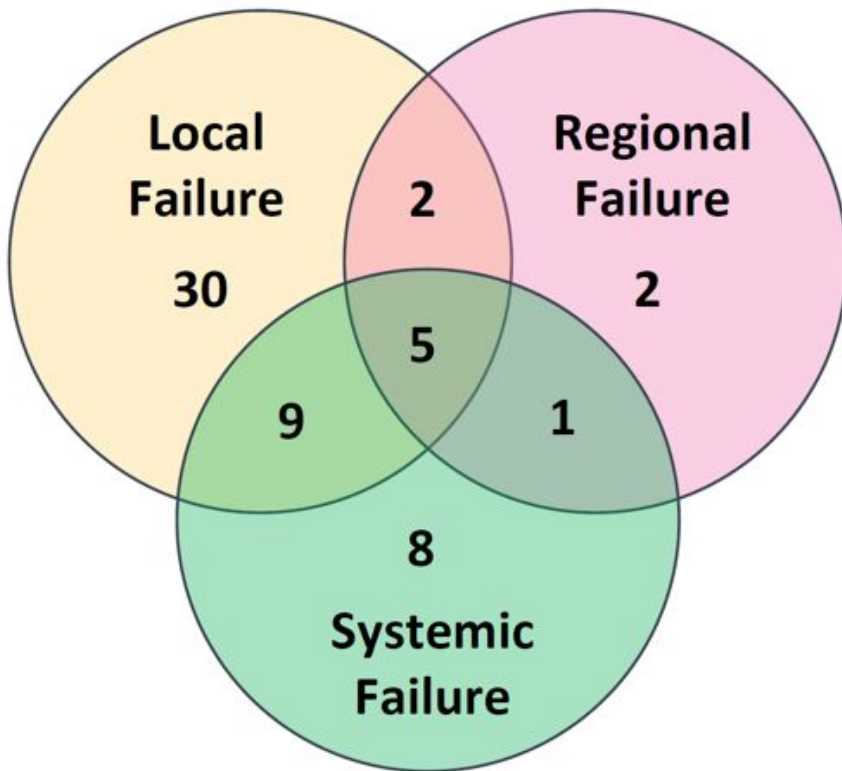
Radiotherapy alone in NK/T cell lymphoma

Author	Pub. Time	n	lesions	Stage	Radiotherapy Dosage	Effects (%)			
						CR	PR	SD	PD
Cheung	2002	18	Nasal	I-II	50Gy	78			22
Kim GE	2001	104	Upper AD tracts	I-II	50-40Gy	69	15	15	
Kim GE	2000	92	Upper AD tracts	I-II	50-40Gy	66	17	16	
Kim K	2006	33	Upper AD tracts	I-II	50Gy	94	0	0	6
Koorn	2004	102	Upper AD tracts	I-II	45Gy	72	14	14	
Chim	2004	7	Upper AD tracts	I-IV	40-50Gy	100	0	0	0
Li CC	2004	11	Nasal	I-IV	44-50Gy	55			
Pan ZH	2006	30	Upper AD tracts	I-IV	91%>40Gy	67	23	7	3
Li YX	2006	66	Nasal	I-II	50Gy	83	9	3	6

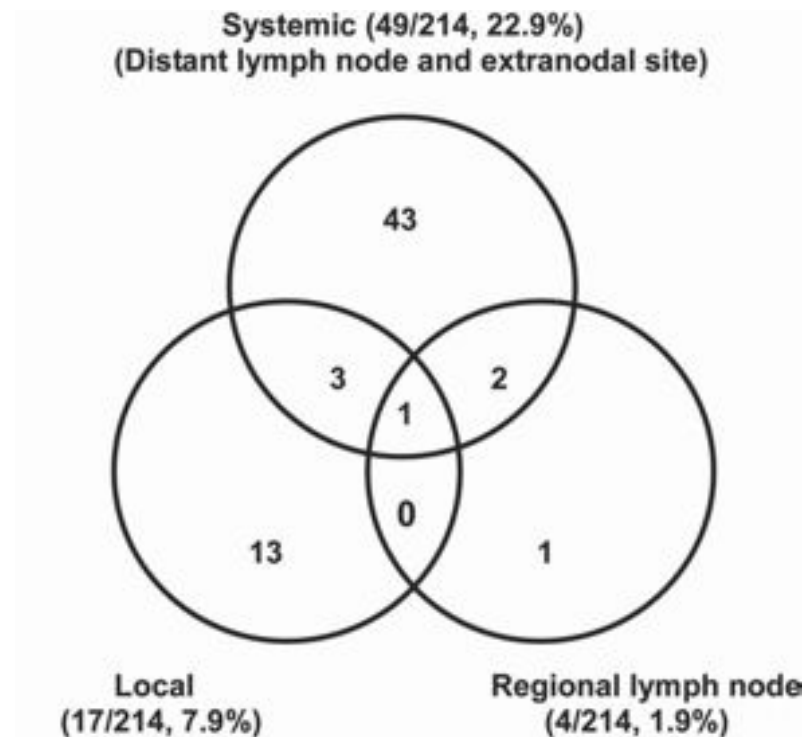
CMT in NK/T cell lymphoma

Author	Pub.time	n	lesions	Stage	Thrapy	5Ys. OS(%)	p
You	2004	46	Nasal	I-II	RT alone: 6	83.3	0.027
					CT+RT: 40	29.5	
Chim	2004	67	Nasal	I-IV	RT alone: 8	83.3	0.03
					CT+RT: 59	32	
Li CC	2004	66	Nasal	I-II	RT alone: 11	60	0.01
					RT+CT: 27	69	
					CT alone: 18	15	
Pan ZH	2006	93	Upper AD tracts	I-IV	CT+RT: 64	30	0.06
					CT alone: 34	0	
He YF	2006	108	Nasal	I-II	CT+RT: 81	60	0.001
					CHOP: 27	20	
Huang MJ	2008	82	Nasal	I-II	RT+CT: 74	62	0.000
					CT alone: 8	12.5	
Au	2008	67	Upper AD tracts	I-II	RT+CT: 34	60	0.045
					CT alone: 23	30	

Treatment failures after radiation therapy of NK/T cell lymphoma patients with stage I / II



N = 92, 1976-1994
5y-OS 40.1%
5y-DFS 37.8%



N=214 (RT 96, RT+CT 118) ,1987-2009
5y-OS 72%, 5y-DFS 65%
5y-LRF 12%, 5y-SF 25.5%, 5y-OF 32.9%

High Systemic failure suggests new chemotherapy should be explored!

L-asparaginase-based salvage regimen for refractory and relapsed ENKTL

- ❑ Refractory and relapsed ENKTL, N=45, 1996-2008
- ❑ 39 pts received RT after CT
- ❑ ORR 82.2% (CR 55.6 %, PR 26.7%)
- ❑ 3 y-OS and 5 y-OS are both 66.9 %
- ❑ The major adverse effects of L-asparaginase were myelosuppression, liver dysfunction hyperglycemia, and allergic reaction

Long-term follow-up results of EPOCH regimen as first-line therapy of NK/T cell lymphoma

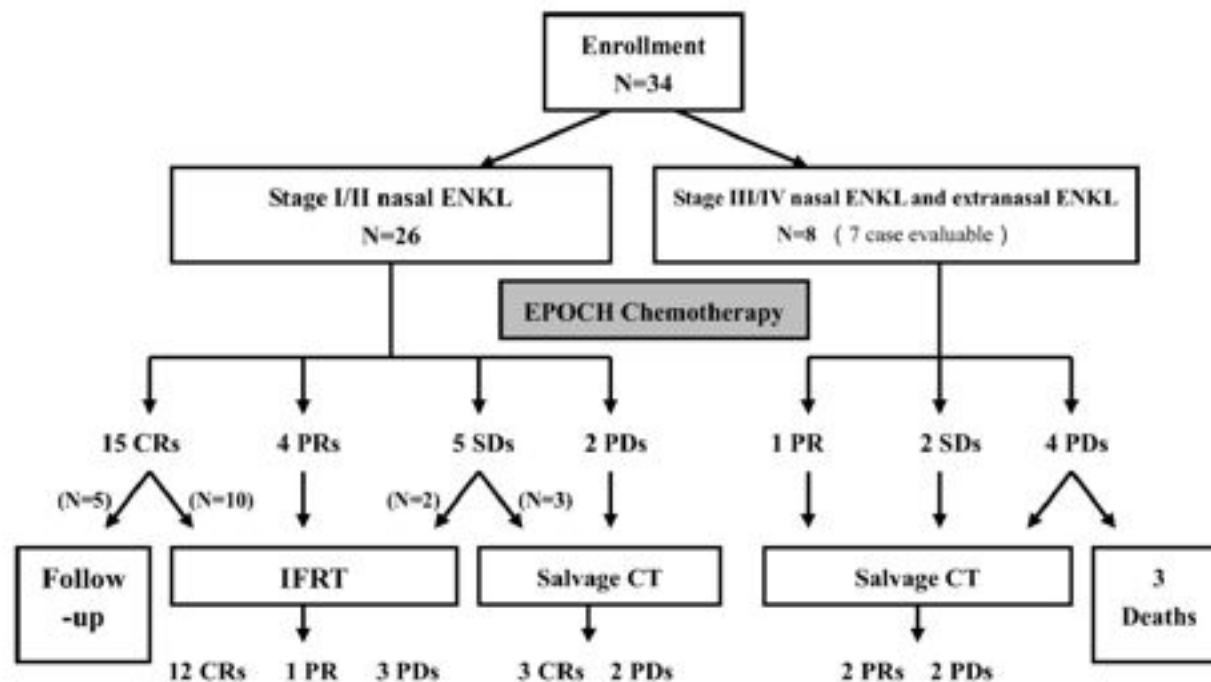


Table II. Objective response to EPOCH chemotherapy.

	<i>n</i>	RR (%)	CR (%)	SD (%)	PD (%)
All patients	33	20 (60.6)	15 (45.5)	7 (21.2)	6 (18.2)
Localized nasal ENKL	26	19 (73.1)	15 (57.7)	5 (19.2)	2 (7.7)
ENKL with extranasal or disseminated lesions	7	1 (14.3)	0 (0)	2 (28.6)	4 (57.1)

Long-term follow-up results of EPOCH regimen as first-line therapy of NK/T cell lymphoma

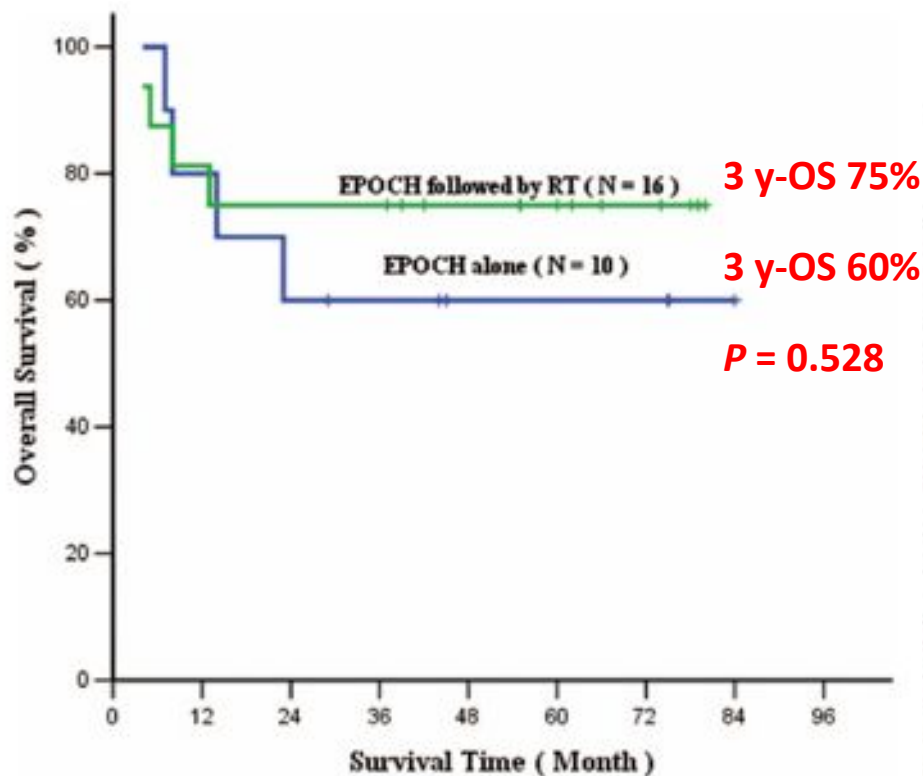


Figure 6. Survival curves of patients with stage I/II nasal ENKL according to first-line treatment modalities.

Table III. Adverse effects of EPOCH chemotherapy.

Toxicity	Grade	
	1/2 (%)	3/4 (%)
Neutropenia	44.1	31.4
Febrile neutropenia	0	15.7
Anemia	15.7	3.9
Thrombocytopenia	34.3	8.8
Nausea/vomiting	39.2	0.0
Diarrhea	0	2.0
Mucitis	3.9	0.0
Alopecia	31.4	4.9
Abnormal transaminase	7.8	0.0
Cardiotoxicity	2.9	0.0
Peripheral neuritis	2.9	0.0

NK/T-cell Lymphoma^a

- Clinical pathological correlation is required to establish diagnosis.
- Optimal first-line therapy is controversial.
- For localized presentation in the nasopharynx:
 - Short course of CHOP or CHOP-like chemotherapy for up to 3 cycles followed by involved field RT
 - SMILE (steroid [dexamethasone/prednisolone], methotrexate, ifosfamide, L-asparaginase and etoposide) followed by involved field RT
 - Dose-adjusted EPOCH for up to 3 cycles followed by involved field RT (category 2B)
- Optimal treatment for advanced NK/T-cell lymphoma is not established. CHOP based chemotherapy is associated with poor outcomes. Consider other aggressive regimens such as:
 - L-asparaginase based regimen
 - SMILE (steroid [dexamethasone/prednisolone], methotrexate, ifosfamide, L-asparaginase and etoposide)

- Clinical patholog

- Optimal first-line

- For localized pre

- Short course c

- SMILE (steroid

- followed by im

- Dose-adjusted

- Optimal treatme

- associated with

- L-asparaginas

- SMILE (steroid

NK/T-CELL TREATMENT REGIMENS

References

SMILE (steroid [dexamethasone/prednisolone], methotrexate, ifosfamide, L-asparaginase and etoposide) followed by involved field RT
Yaemaguchi M, Suzuki R, Kwong YL, et al. Phase I study of dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide (SMILE) chemotherapy for advanced-stage, relapsed or refractory extranodal natural killer (NK)/T-cell lymphoma and leukemia. *Cancer Sci* 2008;99:1016-1020.

IMEP (ifosfamide, methotrexate, etoposide, prednisolone)- SMILES core regimen

Lee KW, Yun T, Kim DW, et al. First-line ifosfamide, methotrexate, etoposide and prednisolone chemotherapy +/- radiotherapy is active in stage I/II extranodal NK/T-cell lymphoma. *Leuk Lymphoma* 2006;47:1274-1282.

Dose-adjusted EPOCH

Huang H, Lin Z, Lin X, et al. Long-term outcomes of patients with newly diagnosed NK/T-cell lymphoma treated by EPOCH regimen. *ASH Annual Meeting Abstracts*. 2009. Abstract 2689.

L-asparaginase based regimen

Yong W, Zheng W, Zhu J, et al. L-asparaginase in the treatment of refractory and relapsed extranodal NK/T-cell lymphoma, nasal type. *Ann Hematol* 2009;88:647-652.

GELOX→IFRT

- ❑ **Untreated IE/IEE NKTL, N=27**
- ❑ **ORR 96.3% (CR 74.1%, PR 22.2%) , PD 0**
- ❑ **3/4 toxicity: leukopenia(33.3%) and thrombocytopenia(29.6%). No treatment related death**
- ❑ **Medial follow-up 27.37 months, PD 25.9 %, 4 cases of death**
- ❑ **2-year OS and PFS are both 86 %, 3-year OS and PFS are 78% and 75%, respectively**

Poor prognostic factors of NK/T cell lymphoma

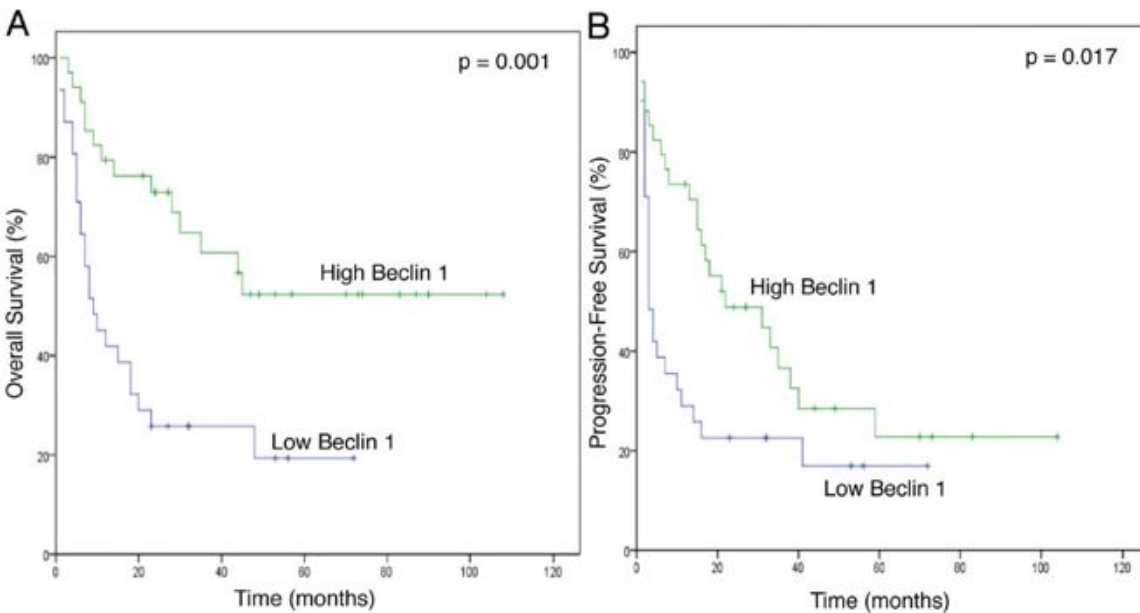
- ☐ Age > 60
- ☐ B symptoms
- ☐ ECOG PS 2
- ☐ LDH ↑
- ☐ Local lymph nodes involvement
- ☐ LTI, bone or cutaneous involvement
- ☐ High Ki-67 expression
- ☐ EBV DNA copy numbers $\geq 6.1 \times 10^7/\text{ml}$

Prognostic factors research in China

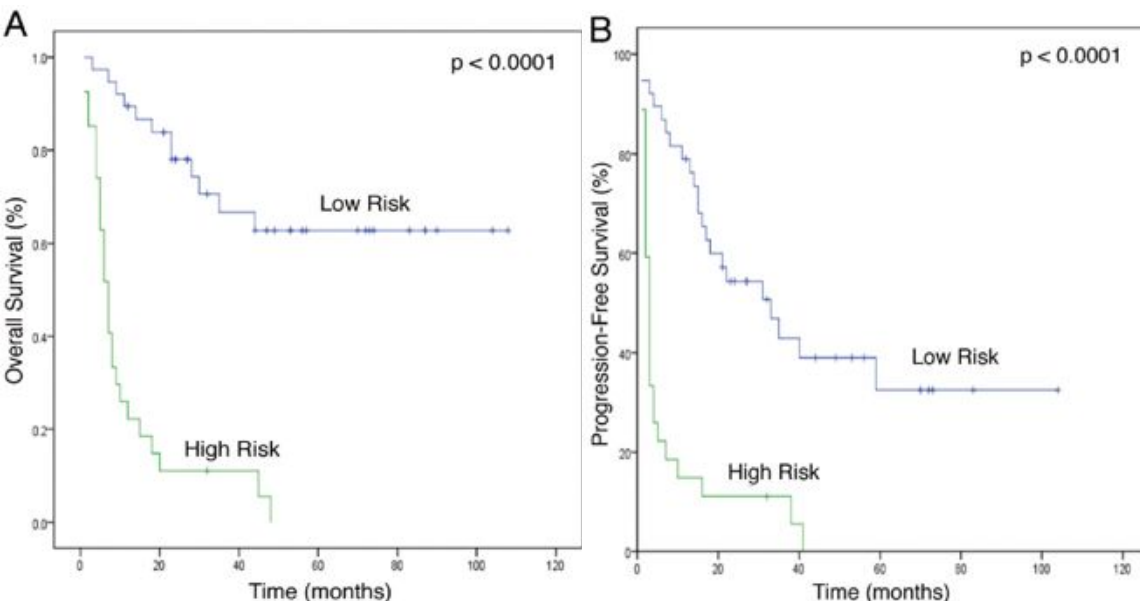
- ☐ **Beclin-1**
- ☐ **Absolute lymphocyte count (ALC)**
- ☐ **β_2 -MG**



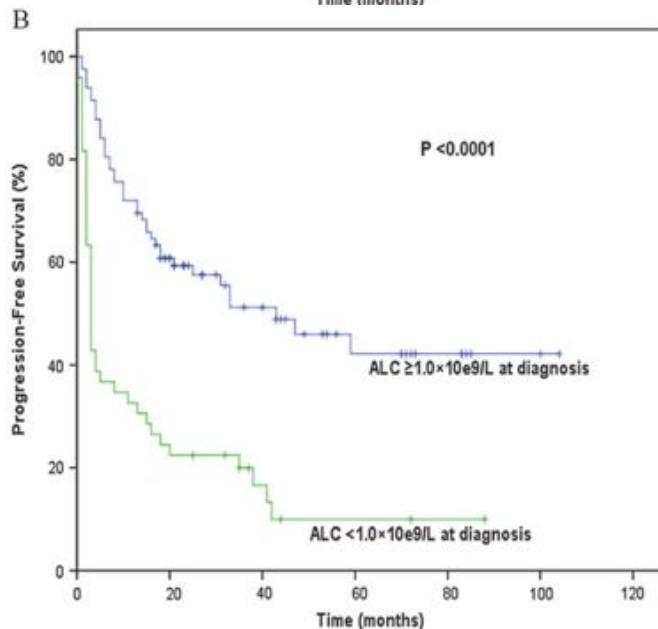
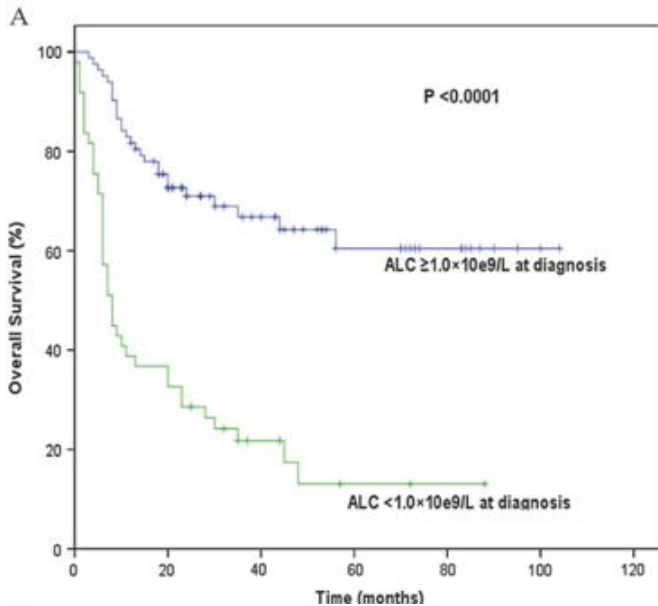
Beclin 1



- ☐ N = 65
- ☐ In this series, more than 80% of patients were in low-risk IPI category, but some of them with poor prognosis
- ☐ Low Beclin 1 expression showed a significant association with the advanced stage and intermediate to high IPI risk
- ☐ Our model placed patients into different risk categories with superior predictive value than IPI



Absolute lymphocyte count (ALC)



- ❑ N = 128
- ❑ Patients with low ALC ($< 1.0 \times 10^9/L$) at diagnosis tended to have more adverse clinical features
- ❑ Using the IPI, PTI, or KPI for nasal NK/T-cell lymphoma, the majority of patients were in the low-risk category (with no or one adverse factor). ALC was helpful to differentiate the low-risk patients with different survival outcomes.

β_2 -MG

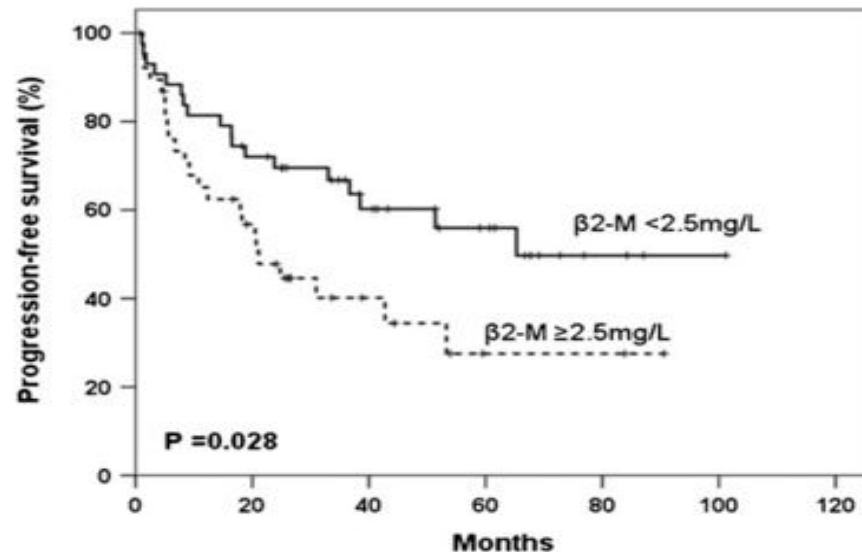
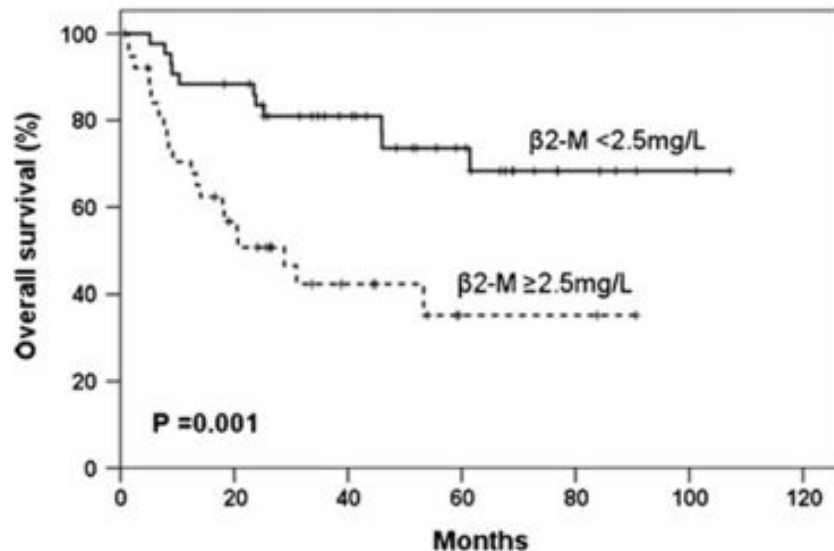


Table 2 Multivariate analysis for OS and PFS in patients with UNKTL

Parameters	Relative risk (RR)	95% Confidence index (CI)		<i>p</i> value
		Lower	Upper	
Overall survival (OS)				
β2-M ≥2.5 mg/L	3.332	1.575	7.047	0.002
IPI score (3–5)	3.091	1.167	8.191	0.023
Progression-free survival (PFS)				
β2-M ≥2.5 mg/L	1.938	1.033	3.635	0.039
IPI score (3–5)	2.631	1.023	6.763	0.045

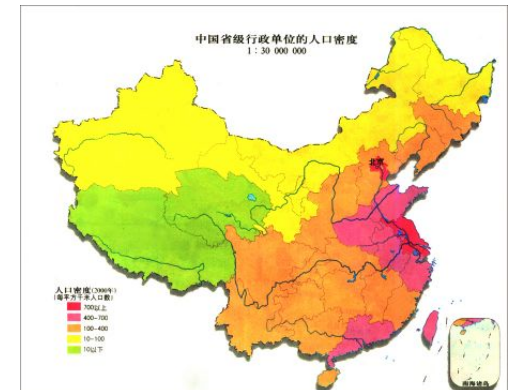
□ $N = 82$

□ Serum $\beta_2\text{-MG} \geq 2.5 \text{ mg/L}$ was significantly associated with poor OS and PFS

□ For patients with early stage, serum $\beta_2\text{-MG}$ at diagnosis could also help to distinguish those with favorable outcomes from those with poor outcomes.

Conclusion

- ❑ The most important task of Chinese Committee of Lymphoma: Promoting and improving the standardize of the diagnosis & treatment of lymphoma in different hospitals
- ❑ Very big differences in frequencies of lymphoma subtypes between China and western countries
- ❑ So far there is no standardize treatment method for NK/T cell ymphoma. Further investigation is required
- ❑ Welcome your collaborations!



主办单位：中国抗癌协会淋巴瘤专业委员会

承办单位：天津医科大学附属肿瘤医院

协办单位：爱荷华大学医学中心

Sponsored by the Chinese Association of Cancer (CACA)
Organized by the University Cancer Institute

中美淋巴瘤和白血病研究中心
Sino-US Center for Lymphoma and Leukemia



Nebraska
Medical Center

**Sino-US Center of Lymphoma and
Leukemia (Tianjin, 2009)**

Sun Yat-sen University Cancer Center, Guangzhou, 1500 beds by the end of 2012



Thank you for attention !