

# Ca Nasopharynx- Management

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# Composite Group

Stage	Ca Nasopharynx
Stage I	T1N0
Stage II	T2N0,T1N1&T2N1
Stage III	T3 or any N2
Stage IVa	T4 or N3
Stage IVb	M1
Stage IVc	NA

# Elective upper-neck versus whole-neck irradiation of the uninvolved neck in patients with nasopharyngeal carcinoma: an open-label, non-inferiority, multicentre, randomised phase 3 trial



Ling-Long Tang\*†, Cheng-Long Huang\*, Ning Zhang\*, Wei Jiang\*, Yi-Shan Wu\*, Shao Hui Huang, Yan-Ping Mao, Qing Liu, Ji-Bin Li, Shao-Qiang Liang, Guan-Jie Qin, Wei-Han Hu, Ying Sun, Fang-Yun Xie, Lei Chen†, Guan-Qun Zhou†, Jun Ma†

- N0 or N1 nodes
- N=446
- Regional relapse free survival



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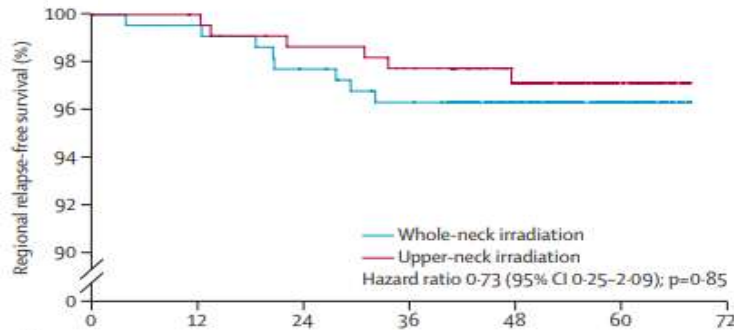
WNI of uninvolved Neck



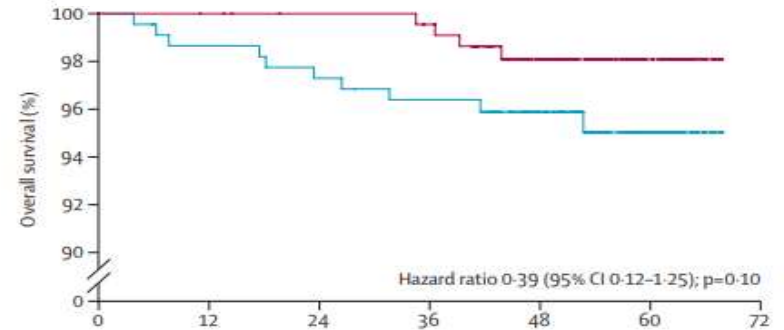
UNI of uninvolved Neck

Lancet Oncol 2022; 23: 479–90

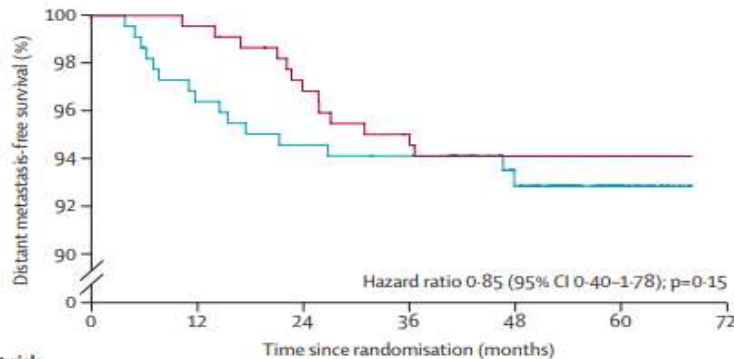
# Median follow-up -53 months



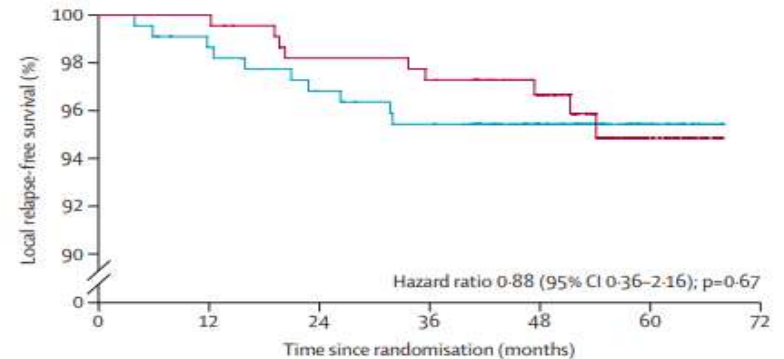
Number at risk (number censored)		Time since randomisation (months)					
	0	12	24	36	48	60	72
Whole-neck irradiation	222 (0)	218 (3)	211 (3)	204 (4)	143 (61)	43 (100)	0 (43)
Upper-neck irradiation	224 (0)	223 (1)	217 (3)	213 (2)	150 (62)	47 (103)	0 (47)



Number at risk (number censored)		Time since randomisation (months)					
	0	12	24	36	48	60	72
Whole-neck irradiation	222 (0)	218 (1)	214 (1)	210 (2)	146 (63)	45 (100)	0 (45)
Upper-neck irradiation	224 (0)	223 (1)	220 (3)	218 (1)	151 (64)	47 (104)	0 (47)

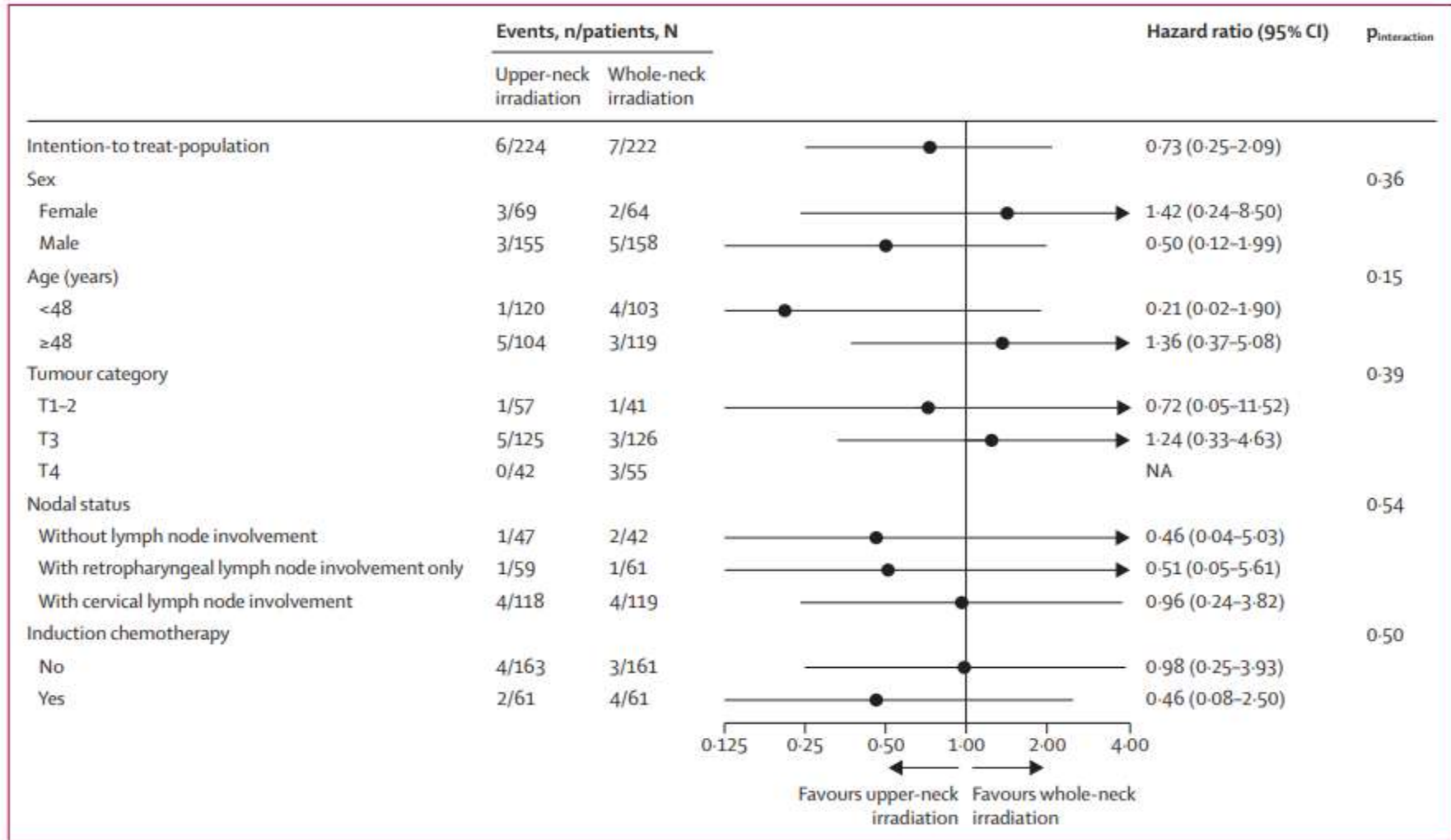


Number at risk (number censored)		Time since randomisation (months)					
	0	12	24	36	48	60	72
Whole-neck irradiation	222 (0)	213 (1)	207 (2)	204 (2)	141 (61)	44 (97)	0 (44)
Upper-neck irradiation	224 (0)	222 (1)	214 (3)	208 (1)	145 (61)	47 (98)	0 (47)



Number at risk (number censored)		Time since randomisation (months)					
	0	12	24	36	48	60	72
Whole-neck irradiation	222 (0)	217 (2)	210 (3)	204 (3)	142 (62)	43 (99)	0 (43)
Upper-neck irradiation	224 (0)	223 (1)	216 (3)	212 (2)	148 (63)	44 (102)	0 (44)

# Subset analysis



# Toxicity

	Upper-neck irradiation group (n=222)			Whole-neck irradiation group (n=222)		
	Grade 1-2	Grade 3	Grade 4	Grade 1-2	Grade 3	Grade 4
<b>Any acute toxicities</b>						
Dermatitis	114 (51%)	1 (<1%)	0	123 (55%)	1 (<1%)	0
Mucositis	125 (56%)	20 (9%)	0	131 (59%)	22 (10%)	1 (<1%)
Dry mouth	159 (72%)	0	0	161 (73%)	0	0
Dysphagia	7 (3%)	0	0	14 (6%)	0	0
Weight loss	114 (51%)	0	0	125 (56%)	0	0
Trismus	0	0	0	1 (<1%)	0	0
Subcutaneous oedema	1 (<1%)	0	0	0	0	0
<b>Any late toxicities*</b>						
Skin†	32 (14%)	0	0	55 (25%)	0	0
Neck tissue damage	50 (23%)	0	0	86 (39%)	2 (1%)	0
Hypothyroidism	63 (28%)	3 (1%)	0	84 (38%)	3 (1%)	0
Dysphagia	38 (17%)	0	0	69 (31%)	2 (1%)	0
Hoarseness	3 (1%)	0	0	1 (<1%)	0	0
Dry mouth	153 (69%)	11 (5%)	0	160 (72%)	15 (7%)	0
Trismus	2 (1%)	0	0	5 (2%)	0	0
Auditory	110 (50%)	0	0	137 (62%)	2 (1%)	0
Temporal lobe injury	17 (8%)	0	0	21 (10%)	0	0

Data are n (%). Safety analyses were done in the safety population, comprising all patients who commenced the randomly assigned treatment. \*One patient in the whole-neck irradiation group died within 3 months after radiotherapy and thus the late toxicity analysis included 221 patients in the whole-neck irradiation group. †Grade 1 skin toxicity included slight atrophy, pigmentation change, and some hair loss; grade 2, included patch atrophy, moderate telangiectasia, and total hair loss; grade 3 or 4 skin toxicity was not observed in this trial.

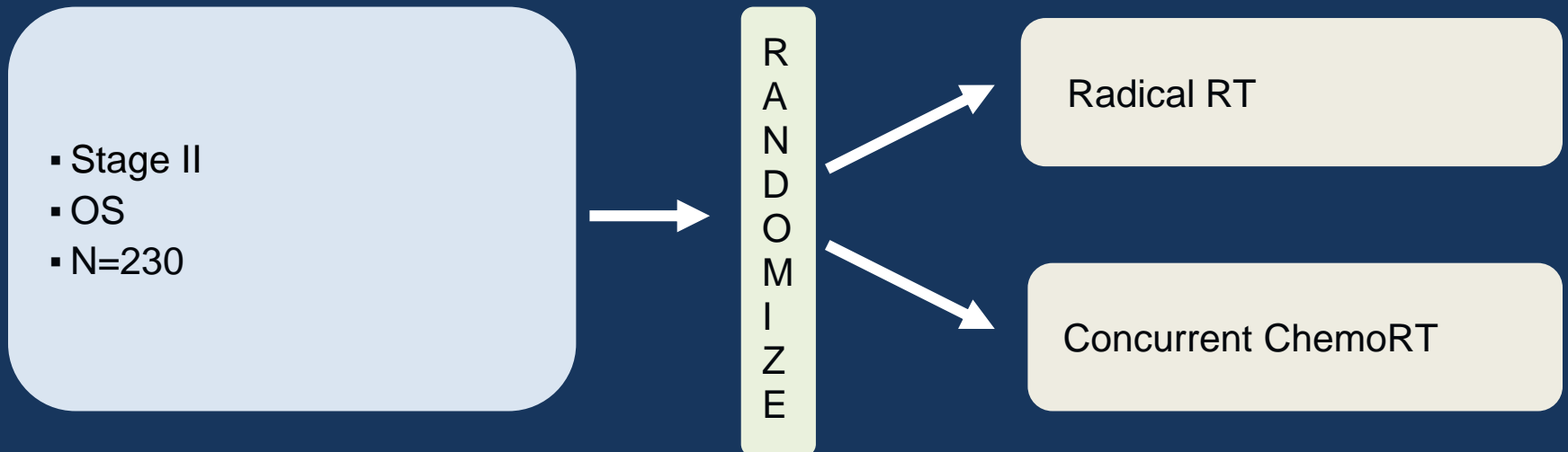
## ARTICLE

# Concurrent Chemoradiotherapy vs Radiotherapy Alone in Stage II Nasopharyngeal Carcinoma: Phase III Randomized Trial

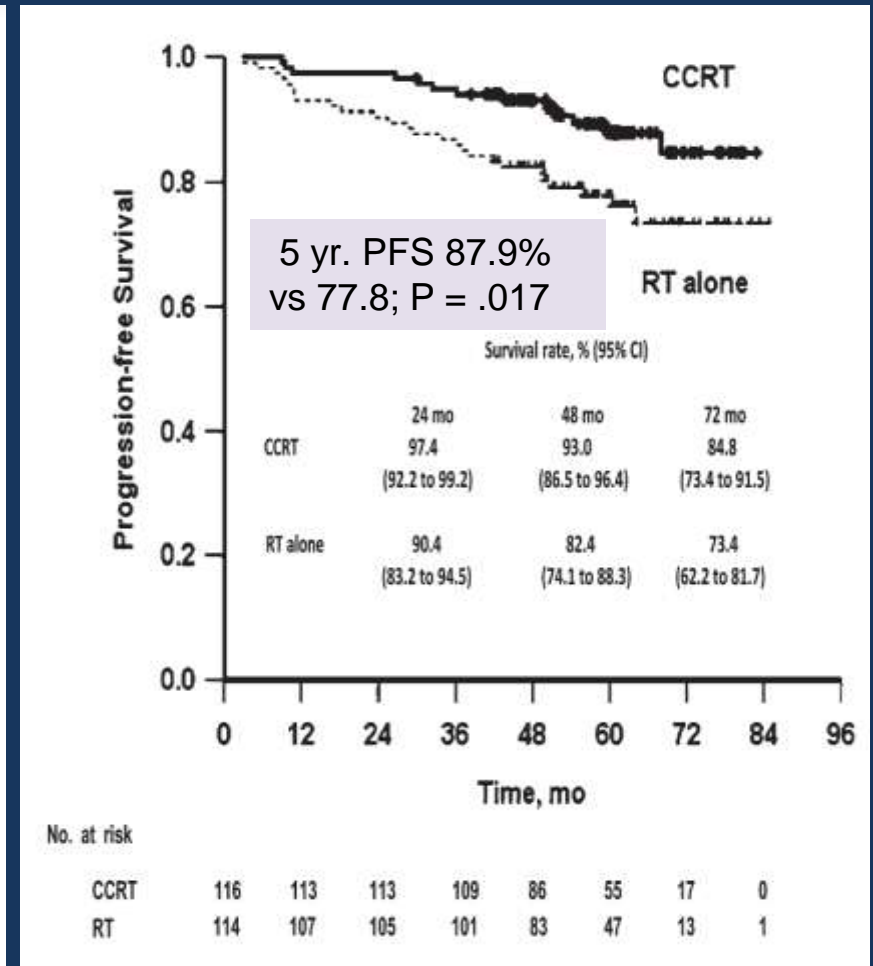
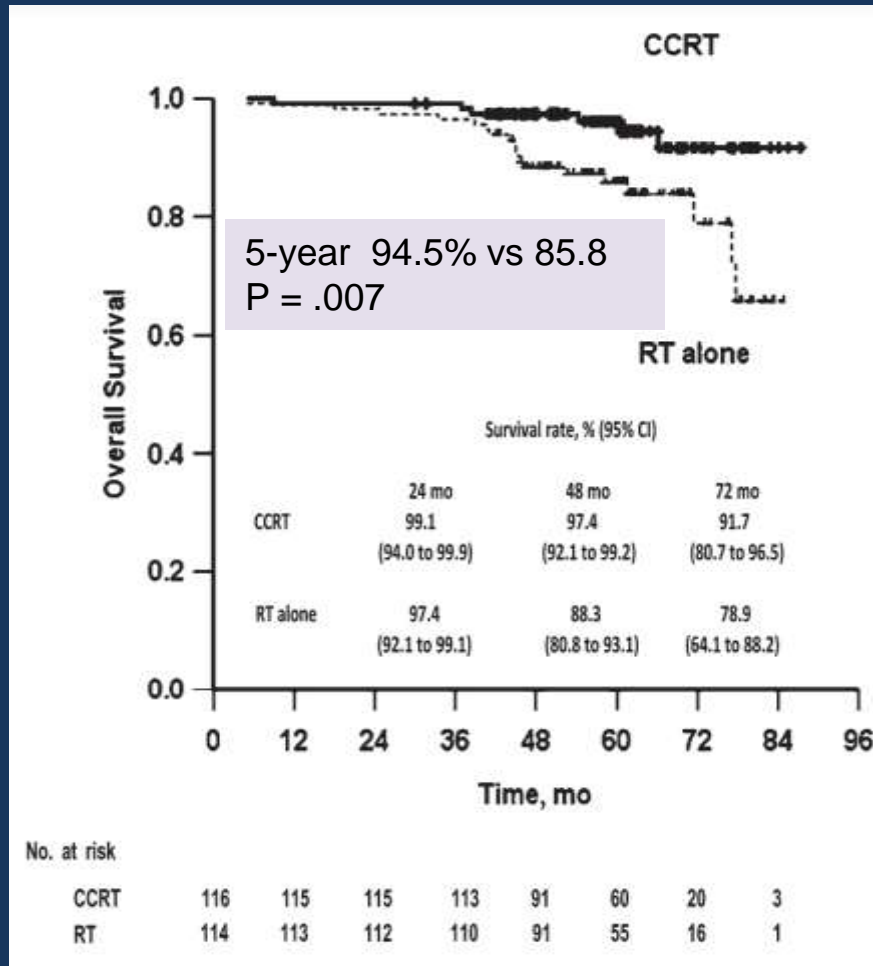
Qiu-Yan Chen, Yue-Feng Wen, Ling Guo, Huai Liu, Pei-Yu Huang, Hao-Yuan Mo, Ning-Wei Li, Yan-Qun Xiang, Dong-Hua Luo, Fang Qiu, Rui Sun, Man-Quan Deng, Ming-Yuan Chen, Yi-Jun Hua, Xiang Guo, Ka-Jia Cao, Ming-Huang Hong, Chao-Nan Qian, Hai-Qiang Mai

Manuscript received April 25, 2011; revised September 15, 2011; accepted September 27, 2011.

**Correspondence to:** Hai-Qiang Mai, MD, PhD, Department of Nasopharyngeal Carcinoma, Sun Yat-sen University Cancer Center, 651 Dongfeng Rd East, Guangzhou 510060, People's Republic of China (e-mail: [maihq@mail.sysu.edu.cn](mailto:maihq@mail.sysu.edu.cn)).

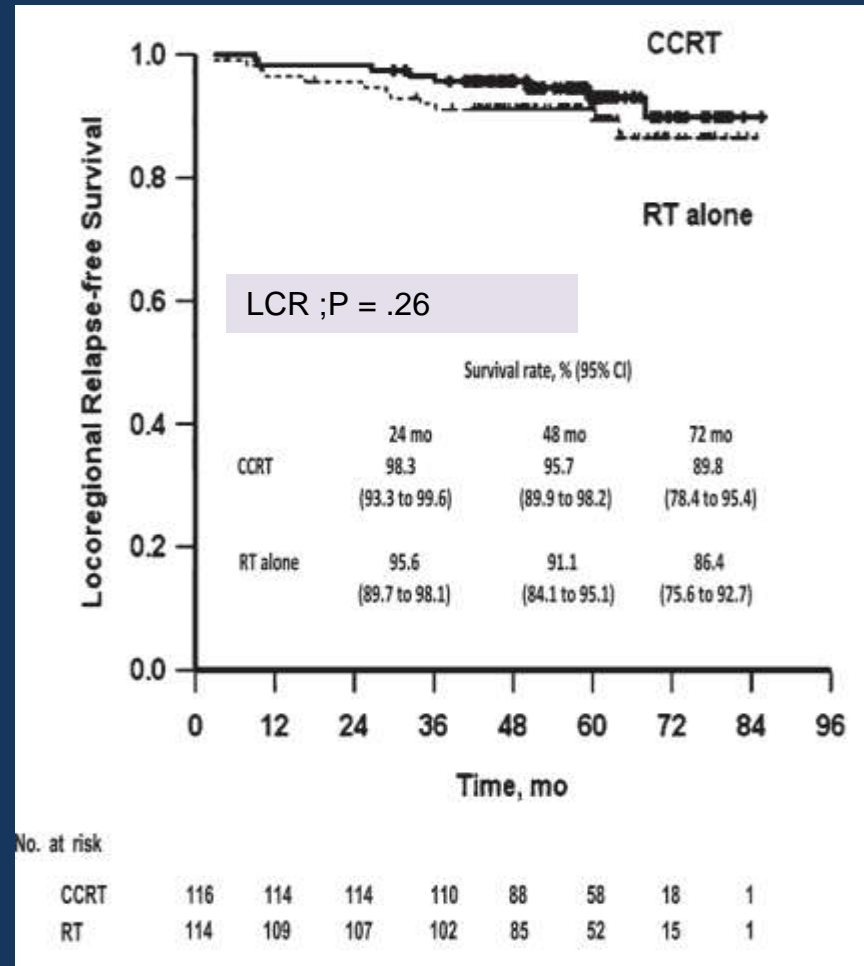
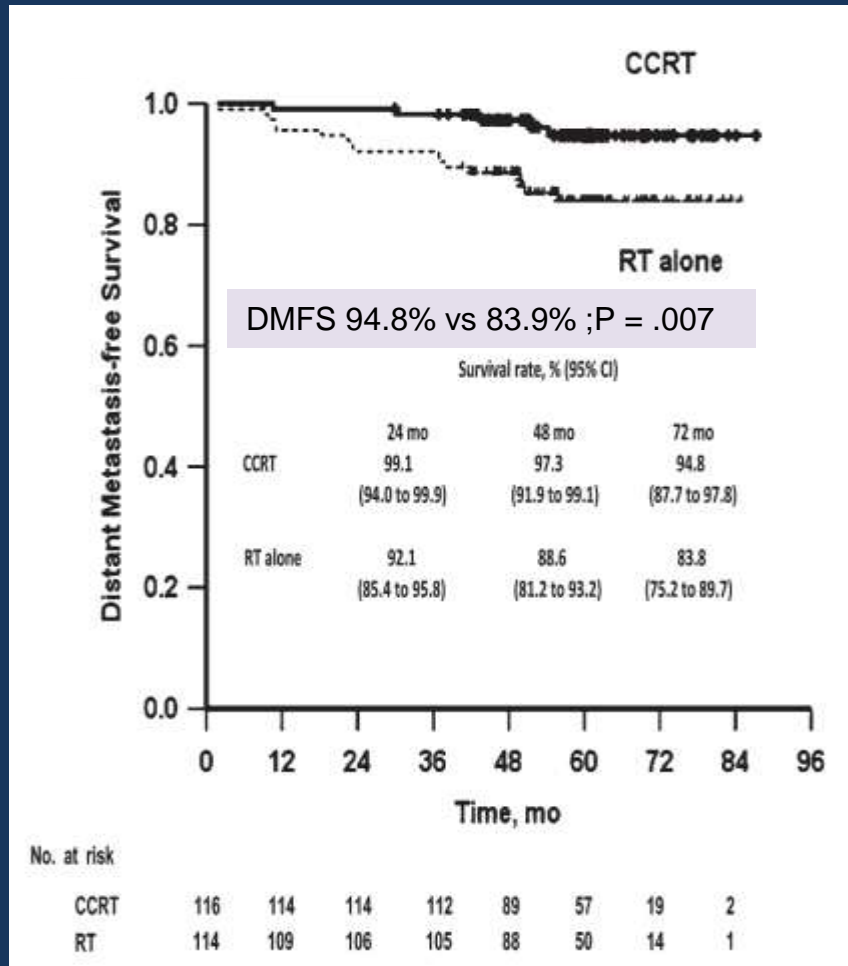


# Median follow up -60 months





# Median follow up -60 months



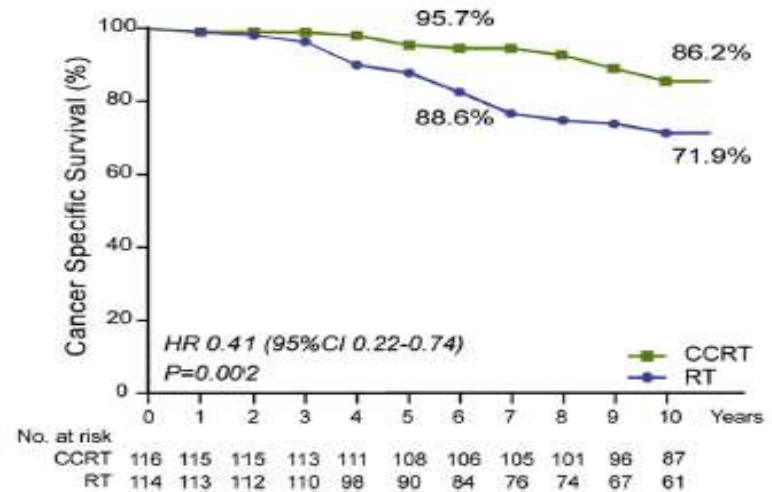
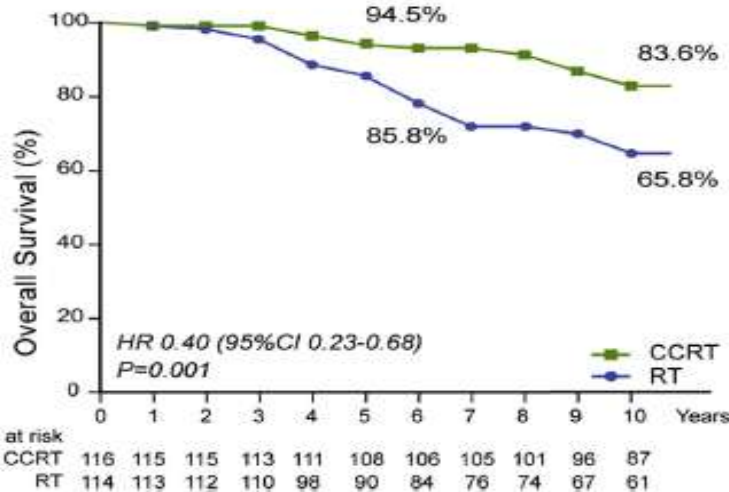


Original Research

# Ten-year outcomes of survival and toxicity for a phase III randomised trial of concurrent chemoradiotherapy versus radiotherapy alone in stage II nasopharyngeal carcinoma



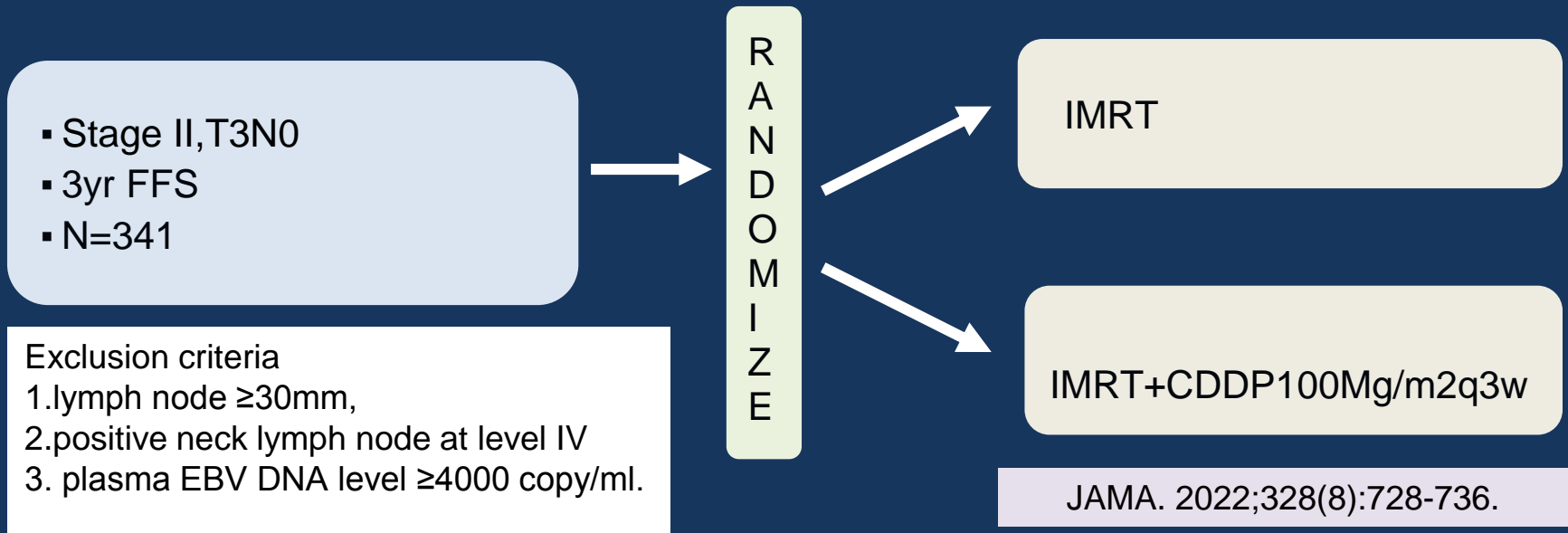
Xiao-Yun Li <sup>a,b,1</sup>, Qiu-Yan Chen <sup>a,b,1</sup>, Xue-Song Sun <sup>a,b</sup>, Sai-Lan Liu <sup>a,b</sup>, Jin-Jie Yan <sup>a,b</sup>, Shan-Shan Guo <sup>a,b</sup>, Li-Ting Liu <sup>a,b</sup>, Hao-Jun Xie <sup>a,b</sup>, Qing-Nan Tang <sup>a,b</sup>, Yu-Jing Liang <sup>a,b</sup>, Yue-Feng Wen <sup>a,b</sup>, Ling Guo <sup>a,b</sup>, Hao-Yuan Mo <sup>a,b</sup>, Ming-Yuan Chen <sup>a,b</sup>, Ying Sun <sup>a,c</sup>, Jun Ma <sup>a,c</sup>, Lin-Quan Tang <sup>a,b,\*\*,2</sup>, Hai-Qiang Mai <sup>a,b,\*,2</sup>



# Effect of Radiotherapy Alone vs Radiotherapy With Concurrent Chemoradiotherapy on Survival Without Disease Relapse in Patients With Low-risk Nasopharyngeal Carcinoma

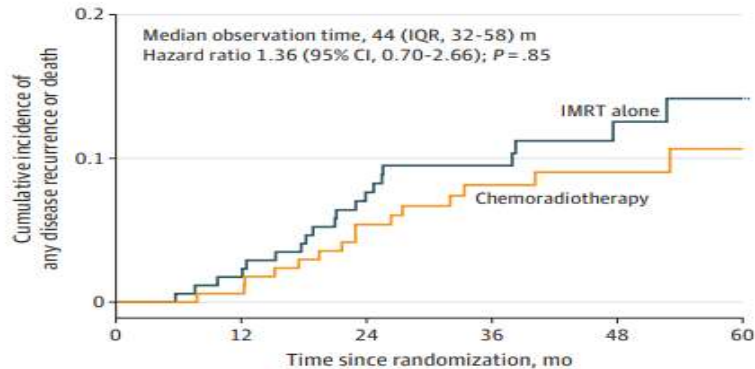
## A Randomized Clinical Trial

Ling-Long Tang, MD; Rui Guo, MD; Ning Zhang, MD; Bin Deng, MD; Lei Chen, MD; Zhi-Bin Cheng, MD; Jing Huang, MD; Wei-Han Hu, MD; Shao Hui Huang, MD; Wei-Jun Luo, MD; Jin-Hui Liang, MD; Yu-Ming Zheng, MD; Fan Zhang, MD; Yan-Ping Mao, MD; Wen-Fei Li, MD; Guan-Qun Zhou, MD; Xu Liu, MD; Yu-Pei Chen, MD; Cheng Xu, MD; Li Lin, MD; Qing Liu, MD, PhD; Xiao-Jing Du, MD; Yuan Zhang, MD; Ying Sun, PhD; Jun Ma, MD



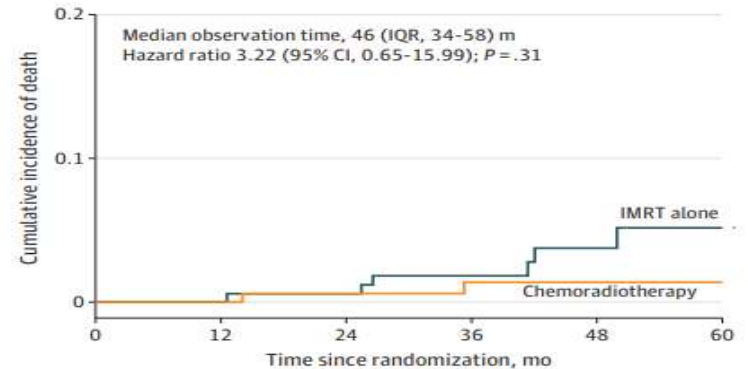
# 3 yr results

Any disease recurrence or death<sup>a</sup>



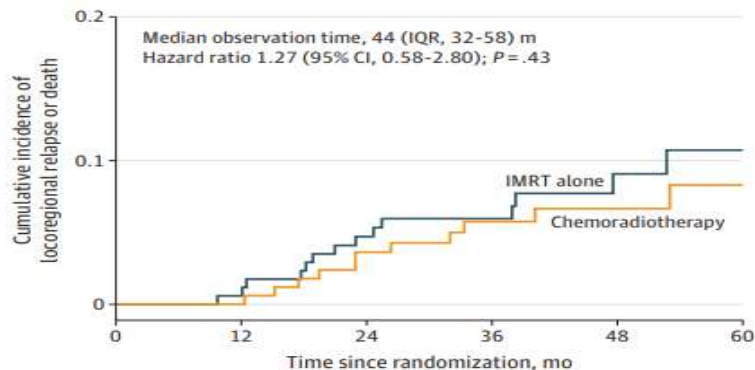
No. at risk	0	12	24	36	48	60
IMRT alone	172	169	150	113	66	30
Concurrent chemoradiotherapy	169	168	153	115	72	31

Death



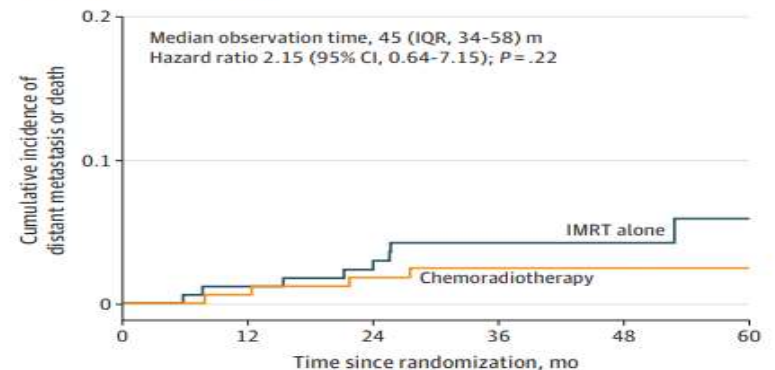
No. at risk	0	12	24	36	48	60
IMRT alone	172	172	162	123	72	31
Concurrent chemoradiotherapy	169	169	161	123	77	35

Locoregional relapse or death



No. at risk	0	12	24	36	48	60
IMRT alone	172	171	154	116	67	30
Concurrent chemoradiotherapy	169	169	155	116	73	32

Distant metastasis or death



No. at risk	0	12	24	36	48	60
IMRT alone	172	170	157	119	70	31
Concurrent chemoradiotherapy	169	168	159	122	76	34

# Toxicity

Event <sup>a</sup>	Group, No. (%) <sup>b</sup>			
	IMRT alone (n = 165)		Concurrent chemoradiotherapy (n = 169)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
<b>Acute toxicities</b>				
<b>Hematologic</b>				
Leukocytes <4000/ $\mu$ L	37 (22)	2 (1)	103 (61)	17 (10)
Hemoglobin <lower limits of normal	27 (16)	0	127 (75)	3 (2)
Neutropenia <2000/ $\mu$ L	12 (7)	3 (2)	60 (36)	11 (7)
Thrombocytopenia <10 <sup>5</sup> / $\mu$ L	2 (1)	1 (1)	41 (24)	1 (1)
<b>Nonhematologic</b>				
Mucositis	116 (70)	16 (10)	113 (67)	32 (19)
Dry mouth	33 (20)	0	50 (30)	0
Dermatitis	31 (19)	0	54 (32)	0
Weight loss	28 (17)	1 (1)	94 (56)	8 (5)
Anorexia	22 (13)	8 (5)	28 (17)	49 (29)
Vomiting	14 (8)	2 (1)	48 (28)	25 (15)
Nausea	14 (8)	1(1)	57 (34)	22 (13)
Dysphagia	5 (3)	1 (1)	22 (13)	3 (2)
Fever	0	0	0	1 (1)

Stage III& IVa



Contents lists available at SciVerse ScienceDirect

## Radiotherapy and Oncology

journal homepage: [www.thegreenjournal.com](http://www.thegreenjournal.com)



Phase III randomised trial

A prospective, randomized study comparing outcomes and toxicities of intensity-modulated radiotherapy vs. conventional two-dimensional radiotherapy for the treatment of nasopharyngeal carcinoma

Gang Peng, Tao Wang, Kun-yu Yang, Sheng Zhang, Tao Zhang, Qin Li, Jun Han, Gang Wu\*

*Cancer Center of Union Hospital, Wuhan, Hubei 430022, PR China*

# 5yr Efficacy results

## 5 yr results

		<i>n</i>	IMRT group ( <i>n</i> = 306)	2D-CRT group ( <i>n</i> = 310)	<i>p</i>
Local control rate (%)	Total	616	90.5 (86.8-94.3)	83.8 (78.8-88.9)	0.046
	T2a	93	94.2 (86.2-100)	94.7 (87.6-100)	0.962
	T2b	183	90.2 (83.8-96.8)	88.4 (80.4-96.5)	0.85
	T3	174	91 (84.5-97.4)	80.6 (70.7-90.6)	0.122
	T4	103	81.5 (68-94.9)	62.2 (45.5-78.9)	0.05
Regional control rate (%)	Total	616	91.7 (88.1-95.4)	84 (78.4-89.4)	0.049
	N1	294	90.2 (83.4-97.1)	84.6 (75.9-93.4)	0.227
	N2	111	93.9 (90-97.8)	74.8 (65.1-84.5)	0.026
	N3	31	91.6 (76.0-100)	89.5 (75.7-100)	0.844
Overall survival (%)	Total	616	79.6 (74.1-85.1)	67.1 (60.1-74.1)	0.001
	Ila	32	92.3 (77.8-100)	85.8 (67.1-100)	0.648
	IIb	104	84.9 (73.5-96.4)	77.7 (62.1-95.7)	0.359
	III	293	79.9 (72.4-87.4)	67.4 (57.6-77.3)	0.018
	IVa	87	72.9 (57.3-88.6)	55.2 (37.2-73.1)	0.057
	IVb	31	42.8 (12.1-73.4)	45.6 (21.1-70.0)	0.586



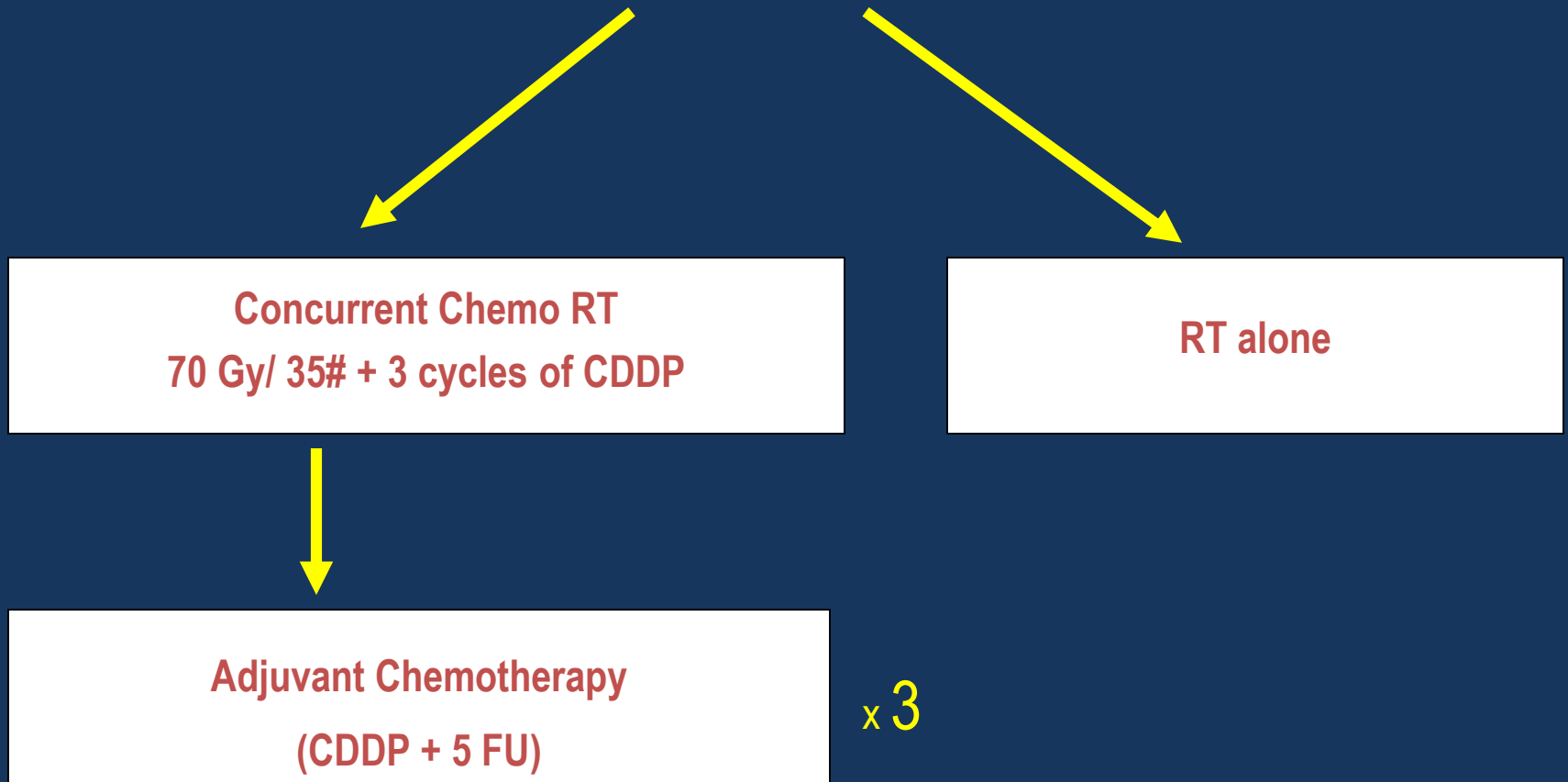
# Acute toxicity

	IMRT group (n = 306)	2D-CRT group (n = 310)	p
<i>Acute complications (%)</i>			
Skin (Grade 3-4)	12.1	16.8	0.109
1	18.3	13.9	
2	69.0	69.0	
3	8.8	11.9	
4	3.3	4.9	
Mucous membrane (Grade 3-4)	33.7	28.7	0.193
1	19.6	18.1	
2	46.4	52.9	
3	25.2	20.6	
4	8.5	8.1	
Xerostomia	83	100	<0.001*
1	54.9	42.6	
2	28.1	54.2	
3	0	3.2	
4	0	0	
Hearing loss	47.4	89	<0.001*

# Late complications

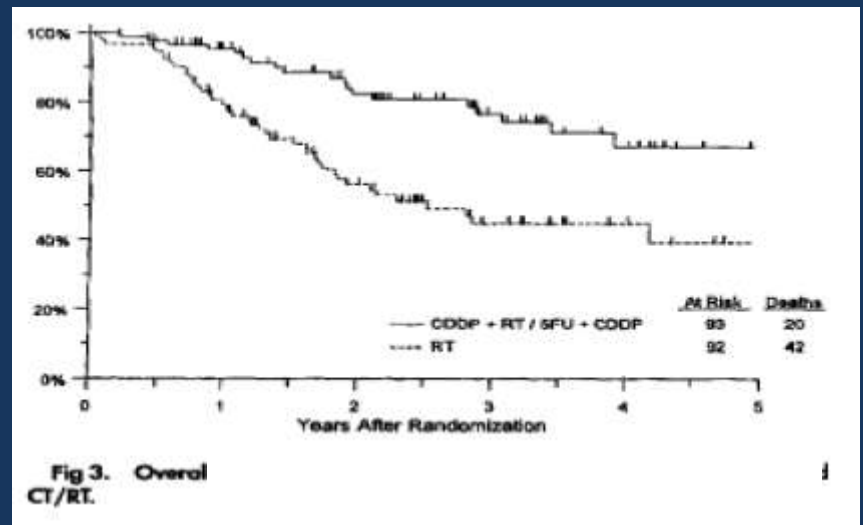
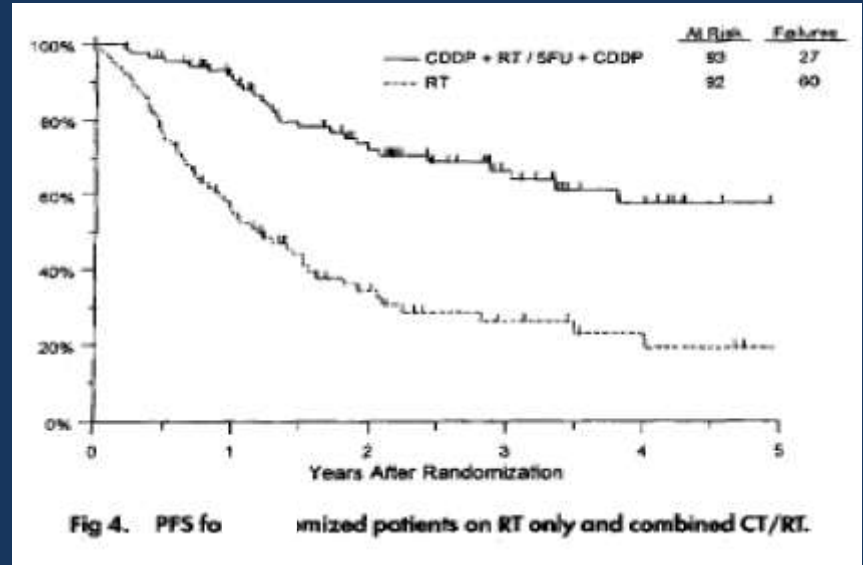
<i>Late complications (%)<sup>a</sup></i>			
Temporal lobe neuropathy	13.1	21	0.010*
Cranial nerve palsy	3.9	8.7	0.020*
Optic nerve/chiasm injury	1.6	3.9	0.138
Brainstem injury	0	0.3	1
Hypopituitarism	2.3	5.2	0.087
Hypothyroidism	1.3	2.9	0.262
Trismus	3.3	13.9	<0.001*
Neck fibrosis	2.3	11.3	<0.001*
Massive bleeding	1	1.6	0.725
Xerostomia	39.5	99.4	<0.001*
1	30.1	69.7	
2	9.5	27.1	
3	0	2.3	
4	0	0.3	
Hearing loss	25.8	84.5	<0.001*

# Intergroup Trial N=193



# U.S. Intergroup 0099

- 3Y PFS 69% (CRT) vs. 24% (RT alone),  $p < 0.001$
- 3Y OS 76% (CRT) vs. 46% (RT alone),  $p = 0.005$



**Randomized Trial of Radiotherapy Versus Concurrent Chemoradiotherapy Followed by Adjuvant Chemotherapy in Patients With American Joint Committee on Cancer/International Union Against Cancer Stage III and IV Nasopharyngeal Cancer of the Endemic Variety**

*Joseph Wee, Eng Huat Tan, Bee Choo Tai, Hwee Bee Wong, Swan Swan Leong, Terence Tan, Eu Tiong Chua, Edward Yang, Khai Mun Lee, Kam Weng Fong, Hoon Seng Khoo Tan, Kim Shang Lee, Susan Loong, Vijay Sethi, Eu Jin Chua, and David Machin*

**Preliminary Results of a Randomized Study on Therapeutic Gain by Concurrent Chemotherapy for Regionally-Advanced Nasopharyngeal Carcinoma: NPC-9901 Trial by the Hong Kong Nasopharyngeal Cancer Study Group**

*Anne W.M. Lee, W.H. Lau, Stewart Y. Tung, Daniel T.T. Chua, Rick Chappell, L. Xu, Lillian Siu, W.M. Sze, T.W. Leung, Jonathan S.T. Sham, Roger K.C. Ngan, Stephen C.K. Law, T.K. Yau, Joseph S.K. Au, Brian O'Sullivan, Ellie S.Y. Pang, S.K. O, Gordon K.H. Au, and Joseph T. Lau*

# Subsequent Asian Trials Contradictory

			3Y OS	Rate of DM
Wee, JCO, 2005 (Singapore)	221 pts WHO type II/II Mostly T3-4 +/-or N2-3	Cis/RT → PF X3	80%	18%
		RT alone	65%	38%
			<i>p=0.0061</i>	<i>p=0.0029</i>
Lee, JCO, 2005 (Hong Kong)	348 pts WHO type II/II Mostly N2-3	Cis/RT → PF X3	78%	24%
		RT alone	78%	27%
			<i>p=0.97</i>	<i>p=0.96</i>

J Clin Oncol 23:6730-6738.

J Clin Oncol 23:6966-6975.



# Meta-analysis in NPC MAC-NPC Collaborative Group

CLINICAL INVESTIGATION

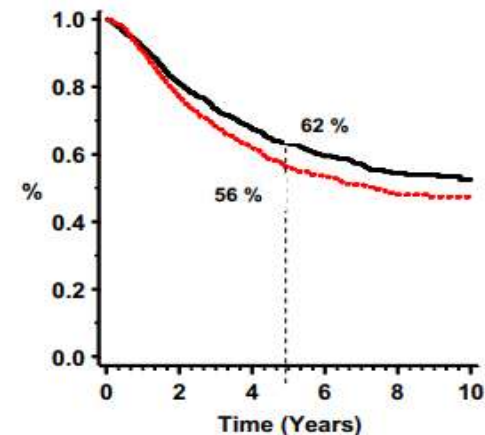
Head and Neck

## CHEMOTHERAPY IN LOCALLY ADVANCED NASOPHARYNGEAL CARCINOMA: AN INDIVIDUAL PATIENT DATA META-ANALYSIS OF EIGHT RANDOMIZED TRIALS AND 1753 PATIENTS

BERTRAND BAUJAT, M.D.,\* HÉLÈNE AUDRY, M.Sc.,\* JEAN BOURHIS, M.D., Ph.D.\*  
ANTHONY T. C. CHAN, M.D.,† HALUK ONAT, M.D.,‡ DANIEL T. T. CHUA, M.D.,§ DORA L. W. KWONG,  
M.D.,§ MUHYI AL-SARRAF, M.D.,|| KWAN-HWA CHI, M.D.,¶ MASATO HAREYAMA, M.D.,#  
SING F. LEUNG, M.D.,† KULLATHORN THEPHAMONGKHOL, M.D.,\* AND  
JEAN-PIERRE PIGNON, M.D., Ph.D.,\* ON BEHALF OF THE MAC-NPC COLLABORATIVE GROUP

\*Institut Gustave-Roussy, Villejuif, France; †Department of Clinical Oncology, Prince of Wales Hospital, Hong-Kong, China; ‡Istanbul University, Institute of Oncology, Istanbul, Turkey; §Department of Clinical Oncology, Queen Mary Hospital, Hong-Kong, China; ||Wayne State University, Detroit, MI; ¶Taiwan Cooperative Oncology Group, Taipei, Taiwan; #Department of Radiology, Sapporo Medical University, Sapporo, Japan

- HR for death=0.82 (95% CI 0.71-0.95)
- 6% absolute survival benefit at 5 years
- Greatest benefit from concurrent chemo  
HR=0.60 (concurrent)  
HR=0.97 (adjuvant)  
HR=0.99 (induction)



Patients at risk

RT+CT	990	730	502	281	120	46
RT alone	985	683	443	237	100	41

**CCRT Vs CCRT followed by Adjuvant chemo?**



# Concurrent chemoradiotherapy plus adjuvant chemotherapy versus concurrent chemoradiotherapy alone in patients with locoregionally advanced nasopharyngeal carcinoma: a phase 3 multicentre randomised controlled trial

Lancet Oncol 2012; 13: 163-71

Lei Chen,<sup>\*</sup> Chao-Su Hu,<sup>\*</sup> Xiao-Zhong Chen,<sup>\*</sup> Guo-Qing Hu, Zhi-Bin Cheng, Yan Sun, Wei-Xiong Li, Yuan-Yuan Chen, Fang-Yun Xie, Shao-Bo Liang, Yong Chen, Ting-Ting Xu, Bin Li, Guo-Xian Long, Si-Yang Wang, Bao-Min Zheng, Ying Guo, Ying Sun, Yan-Ping Mao, Ling-Long Tang, Yu-Ming Chen, Meng-Zhong Liu, Jun Ma

European Journal of Cancer 75 (2017) 150–158



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.ejcancer.com](http://www.ejcancer.com)



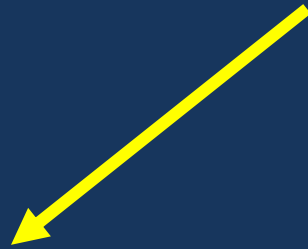
Original Research

## Adjuvant chemotherapy in patients with locoregionally advanced nasopharyngeal carcinoma: Long-term results of a phase 3 multicentre randomised controlled trial



Lei Chen <sup>a,1</sup>, Chao-Su Hu <sup>b,1</sup>, Xiao-Zhong Chen <sup>c,1</sup>, Guo-Qing Hu <sup>d,1</sup>, Zhi-Bin Cheng <sup>e,1</sup>, Yan Sun <sup>f,1</sup>, Wei-Xiong Li <sup>g</sup>, Yuan-Yuan Chen <sup>c</sup>, Fang-Yun Xie <sup>a</sup>, Shao-Bo Liang <sup>h</sup>, Yong Chen <sup>a</sup>, Ting-Ting Xu <sup>b</sup>, Bin Li <sup>c</sup>, Guo-Xian Long <sup>d</sup>, Si-Yang Wang <sup>e</sup>, Bao-Min Zheng <sup>f</sup>, Ying Guo <sup>i</sup>, Ying Sun <sup>a</sup>, Yan-Ping Mao <sup>a</sup>, Ling-Long Tang <sup>a</sup>, Yu-Ming Chen <sup>j</sup>, Meng-Zhong Liu <sup>a</sup>, Jun Ma <sup>a,\*</sup>

**Stage III-Stage IVb  
N=508**



**Concurrent Chemo RT  
70 Gy/ 35# + CDDP Weekly 40mg/m2**

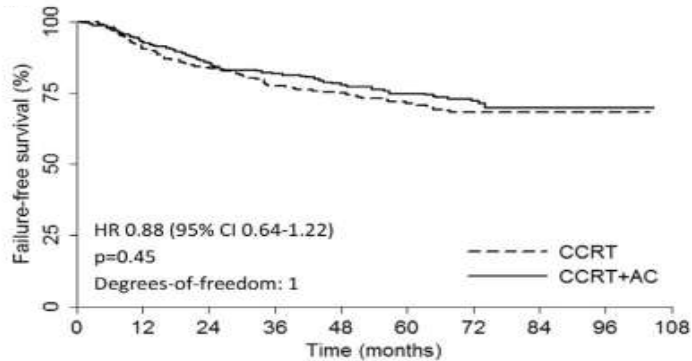
**Concurrent Chemo RT**



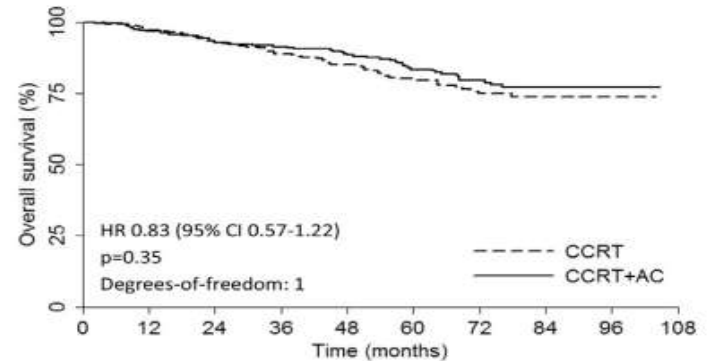
**Adjuvant Chemotherapy  
(CDDP 80mg/m2+ 5 FU 800mg/m2 D1-D4  
q4weeks )**

**x 3**

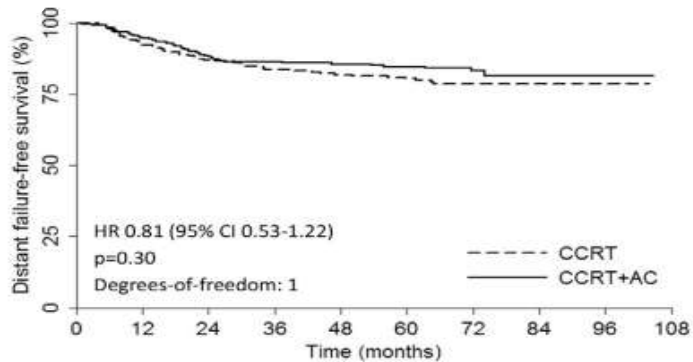
# Median follow up 68.4 months



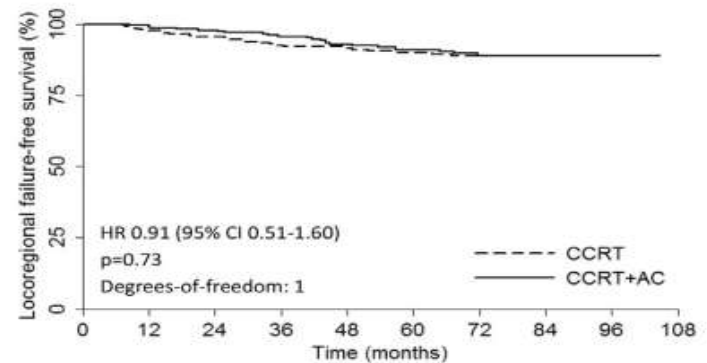
Number at risk		0	12	24	36	48	60	72	84	96	108
CCRT	257	231	212	187	176	150	91	28	8	0	
CCRT+AC	251	230	207	195	182	163	105	28	10	0	



Number at risk		0	12	24	36	48	60	72	84	96	108
CCRT	257	248	236	215	200	168	99	30	8	0	
CCRT+AC	251	239	224	218	203	178	112	31	10	0	



Number at risk		0	12	24	36	48	60	72	84	96	108
CCRT	257	234	216	195	183	159	94	29	8	0	
CCRT+AC	251	231	209	202	189	170	108	30	10	0	

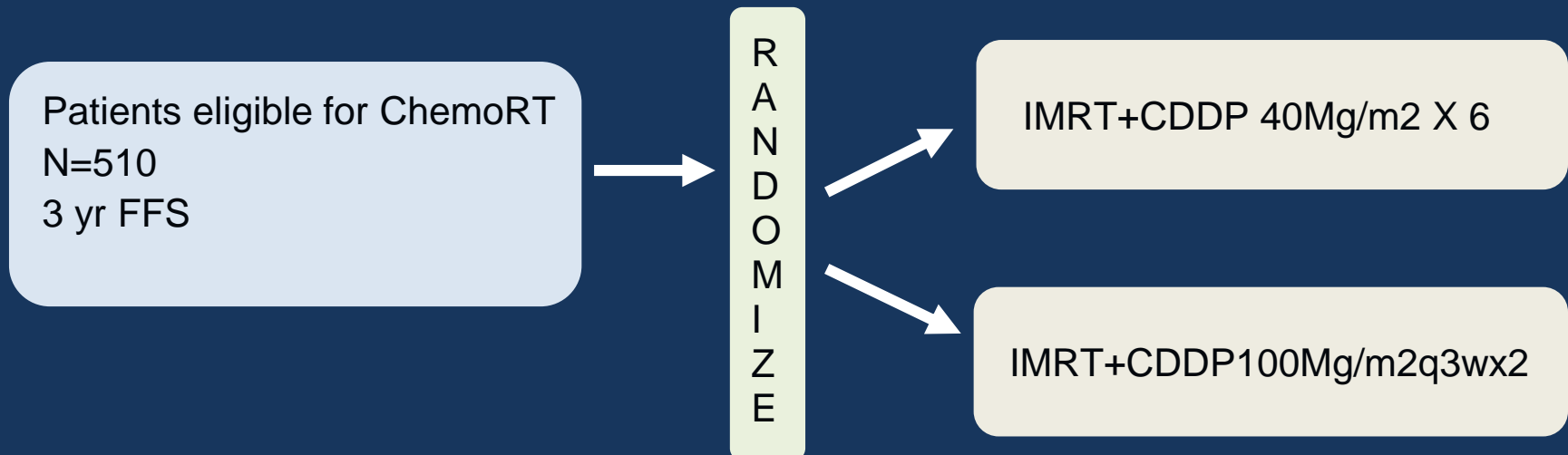


Number at risk		0	12	24	36	48	60	72	84	96	108
CCRT	257	243	230	206	191	158	96	29	8	0	
CCRT+AC	251	238	221	210	196	171	108	29	10	0	

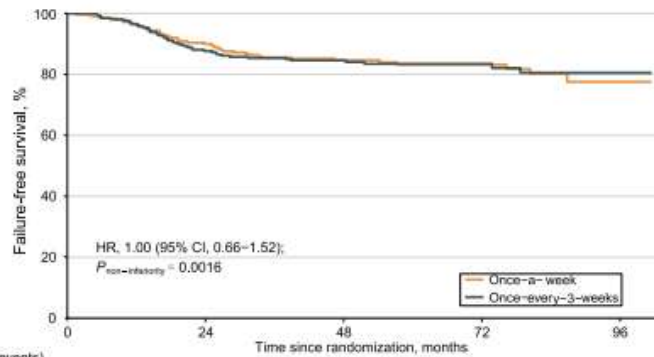
## A Randomized Controlled Trial Comparing Two Different Schedules for Cisplatin Treatment in Patients with Locoregionally Advanced Nasopharyngeal Cancer



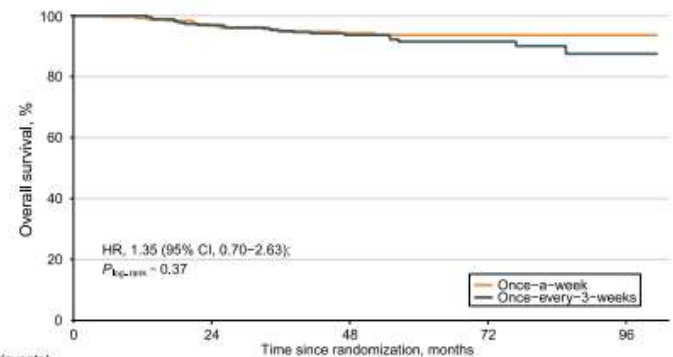
Wei-Xiong Xia<sup>1,2</sup>, Xing Lv<sup>1,2</sup>, Hu Liang<sup>1,2</sup>, Guo-Ying Liu<sup>1,2,3</sup>, Rui Sun<sup>1,2</sup>, Qi Zeng<sup>4</sup>, Si-Wei Li<sup>5</sup>, Hao-Yuan Mo<sup>1,2</sup>, Fei Han<sup>1,2</sup>, Dong-Hua Luo<sup>1,2</sup>, Qing Liu<sup>6</sup>, Meng-Yun Shi<sup>3</sup>, Yan-Fang Ye<sup>3</sup>, Jing Yang<sup>7</sup>, Liang-Ru Ke<sup>1,2</sup>, Meng-Yun Qiang<sup>1,2</sup>, Wen-Ze Qiu<sup>1,2</sup>, Ya-Hui Yu<sup>1,2</sup>, Kui-Yuan Liu<sup>1,2</sup>, Xin-Jun Huang<sup>1,2</sup>, Wang-Zhong Li<sup>1,2</sup>, Shu-Hui Lv<sup>1,2</sup>, Zhuo-Chen Cai<sup>1,2</sup>, Jing-Jing Miao<sup>1,2</sup>, Ling Guo<sup>1,2</sup>, Ming-Yuan Chen<sup>1,2</sup>, Ka-Jia Cao<sup>1,2</sup>, Lin Wang<sup>1,2</sup>, Chong Zhao<sup>1,2</sup>, Pei-Yu Huang<sup>1,2</sup>, Qiu-Yan Chen<sup>1,2</sup>, Yi-Jun Hua<sup>1,2</sup>, Lin-Quan Tang<sup>1,2</sup>, Chao-Nan Qian<sup>1,2</sup>, Hai-Qiang Mai<sup>1,2</sup>, Xiang Guo<sup>1,2</sup>, and Yan-Qun Xiang<sup>1,2</sup>



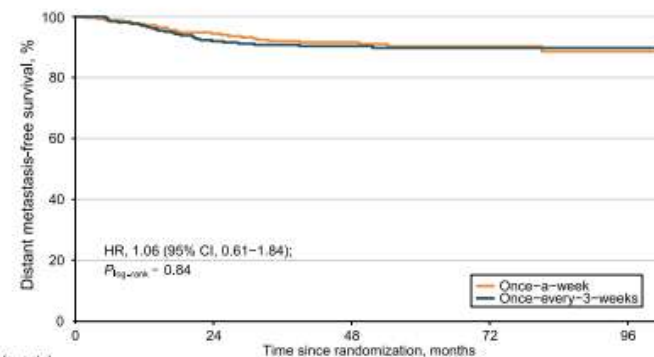
# Median follow up 58.3 months



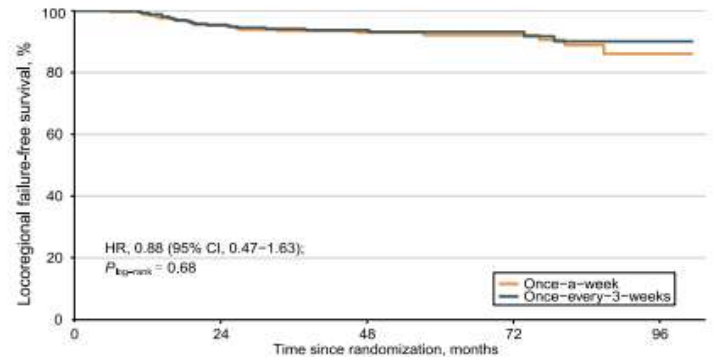
No. at risk (events)	0	24	48	72	96
Once-a-week	250 (0)	244 (25)	160 (38)	64 (40)	7 (43)
Once-every-3-weeks	260 (0)	227 (32)	162 (40)	62 (42)	9 (44)



No. at risk (events)	0	24	48	72	96
Once-a-week	250 (0)	241 (8)	176 (14)	68 (15)	8 (15)
Once-every-3-weeks	260 (0)	251 (6)	179 (16)	69 (19)	11 (21)



No. at risk (events)	0	24	48	72	96
Once-a-week	250 (0)	233 (14)	168 (21)	66 (23)	7 (24)
Once-every-3-weeks	260 (0)	236 (21)	170 (25)	65 (26)	10 (26)



No. at risk (events)	0	24	48	72	96
Once-a-week	250 (0)	231 (11)	168 (17)	66 (18)	7 (21)
Once-every-3-weeks	260 (0)	240 (12)	171 (16)	66 (17)	10 (19)

# Toxicity

Adverse event	OAW (N = 249)		OETW (N = 260)		P
	Grade 3	Grade 4	Grade 3	Grade 4	
Acute toxicity					
<i>Hematologic</i>					
Anemia	8 (3.2%)	2 (0.8%)	4 (1.5%)	1 (0.4%)	0.16
Thrombocytopenia	11 (4.4%)	1 (0.4%)	2 (0.8%)	1 (0.4%)	0.015
Neutropenia	27 (10.8%)	1 (0.4%)	23 (8.8%)	0	0.37
Leucopenia	60 (24.1%)	8 (3.2%)	41 (15.8%)	1 (0.4%)	0.002
<i>Non-hematologic</i>					
Stomatitis/mucositis	89 (35.7%)	0	85 (32.7%)	1 (0.4%)	0.53
Vomiting	28 (11.2%)	0	33 (12.7%)	0	0.62
Nausea	27 (10.8%)	0	30 (11.5%)	0	0.80
Hiccups	10 (4.0%)	0	15 (5.8%)	0	0.36
Constipation	4 (1.6%)	0	4 (1.5%)	0	>0.99 <sup>a</sup>
Diarrhea	4 (1.6%)	0	9 (3.5%)	0	0.18
Dysphagia or odynophagia	7 (2.8%)	0	6 (2.3%)	0	0.72
Dermatitis	15 (6.0%)	0	22 (8.5%)	0	0.29
Xerostomia	16 (6.4%)	—	19 (7.3%)	—	0.69
Weight loss	8 (3.2%)	0	5 (1.9%)	0	0.36
Fever	2 (0.8%)	0	1 (0.4%)	0	0.97 <sup>a</sup>
Ototoxicity	2 (0.8%)	0	3 (1.2%)	0	>0.99 <sup>a</sup>
Neurotoxicity	0	0	1 (0.4%)	0	>0.99 <sup>b</sup>
Atrial fibrillation	1 (0.4%)	0	0	0	0.49 <sup>b</sup>
Stroke	0	0	0	1 (0.4%)	>0.99 <sup>b</sup>
Renal dysfunction	1 (0.4%)	0	0	0	0.49 <sup>b</sup>
Transaminase elevation	6 (2.4%)	0	4 (1.5%)	0	0.70 <sup>a</sup>
Hypokalemia	11 (4.4%)	0	12 (4.6%)	1 (0.4%)	0.76
Hyponatremia	10 (4.0%)	2 (0.8%)	20 (7.7%)	2 (0.8%)	0.10
Hypocalcemia	2 (0.8%)	0	0	0	0.24 <sup>b</sup>
Hypomagnesemia	6 (2.4%)	2 (0.8%)	3 (1.2%)	0	0.11
Any events grade ≥ 3	150 (60.2%)	15 (6%)	138 (53.1%)	7 (2.7%)	0.015
Late toxicity					
Otitis	4 (1.6%)	0	2 (0.8%)	0	0.64 <sup>a</sup>
Ototoxicity	34 (13.7%)	7 (2.8%)	20 (7.7%)	5 (1.9%)	0.021

# Further progress

CCRT

```
graph TD; CCRT[CCRT] --> RAAC[Risk Adapted Adjuvant Chemotherapy]; CCRT --> IC[Induction Chemotherapy]; CCRT --> AC[Adjuvant Chemotherapy Capecitabine];
```

Risk Adapted Adjuvant  
Chemotherapy

Induction Chemotherapy

Adjuvant Chemotherapy  
Capecitabine

## Analysis of Plasma Epstein-Barr Virus DNA in Nasopharyngeal Cancer After Chemoradiation to Identify High-Risk Patients for Adjuvant Chemotherapy: A Randomized Controlled Trial

Anthony T.C. Chan, Edwin P. Hui, Roger K.C. Ngan, Stewart Y. Tung, Ashley C.K. Cheng, Wai T. Ng, Victor H.F. Lee, Brigitte B.Y. Ma, Hoi C. Cheng, Frank C.S. Wong, Herbert H.F. Loong, Macy Tong, Darren M.C. Poon, Anil T. Ahuja, Ann D. King, Ki Wang, Frankie Mo, Benny C.Y. Zee, K.C. Allen Chan, and Y.M. Dennis Lo

### Hong Kong NPC Study Group 0502 Trial (NCT00370890)



- UICC stage IIB, III, IVA or IVB NPC
- No clinical and radiological evidence of distant metastasis at diagnosis (M0)
- detectable plasma EBV-DNA at 6-8 weeks after completion of RT or CRT
- No clinical evidence of persistent loco-regional disease after primary treatment
- ECOG 0 or 1

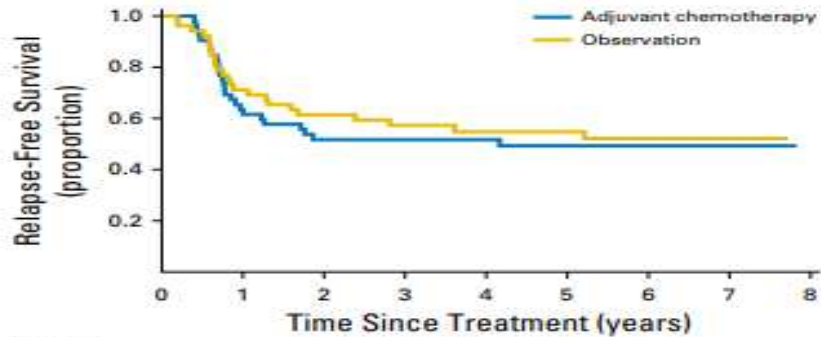
R  
A  
N  
D  
O  
M  
I  
S  
E

Stratification:  
- RT vs CRT  
- Stage II/III vs IV

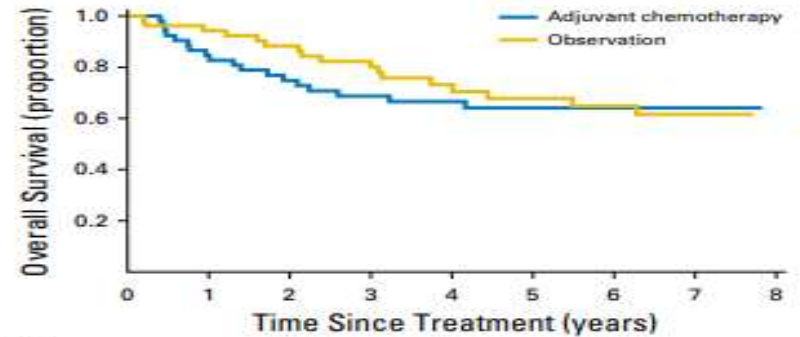
EBV-DNA PET/CT (0 month)	Adjuvant Chemotherapy	EBV-DNA PET/CT (6 months)
<b>Arm A</b>		
✓ ✓	Chemotherapy (Cisplatin-gemcitabine x 6)	✓ ✓
<b>Arm B</b>		
✓ ✓	No chemotherapy	✓ ✓



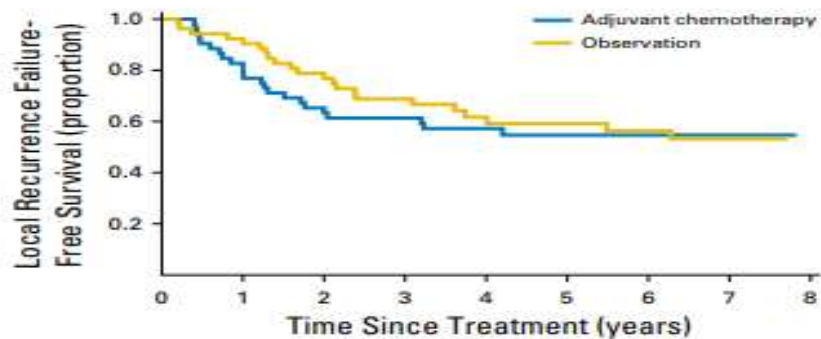
# Efficacy



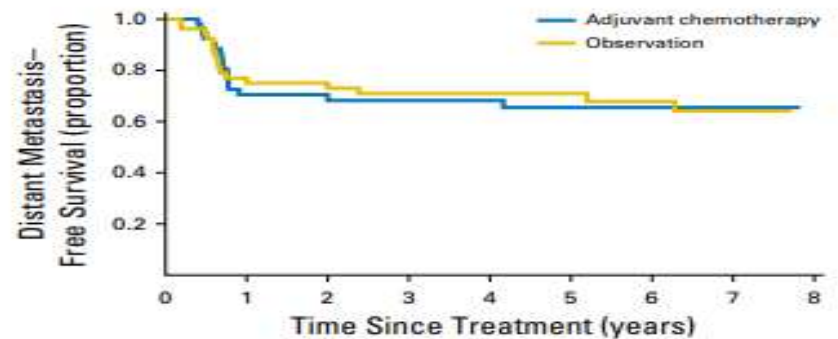
No. at risk		0	1	2	3	4	5	6	7	8
Adjuvant chemotherapy	52	34	27	26	23	19	16	12	8	6
Observation	52	38	32	27	21	21	18	14	9	9



No. at risk		0	1	2	3	4	5	6	7	8
Adjuvant chemotherapy	52	45	38	34	28	24	20	14	8	8
Observation	52	50	45	39	28	25	22	14	9	9

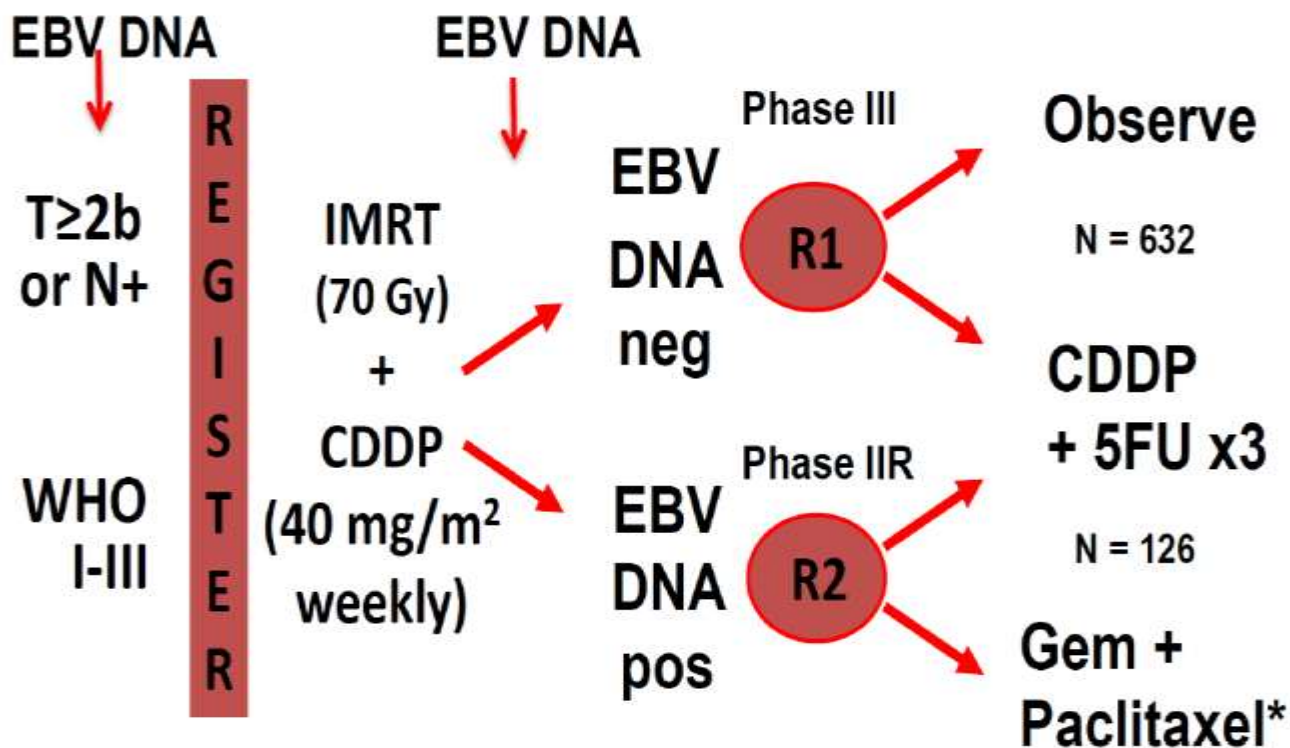


No. at risk		0	1	2	3	4	5	6	7	8
Adjuvant chemotherapy	52	43	33	30	24	20	17	12	6	6
Observation	52	48	40	33	25	23	20	14	9	9



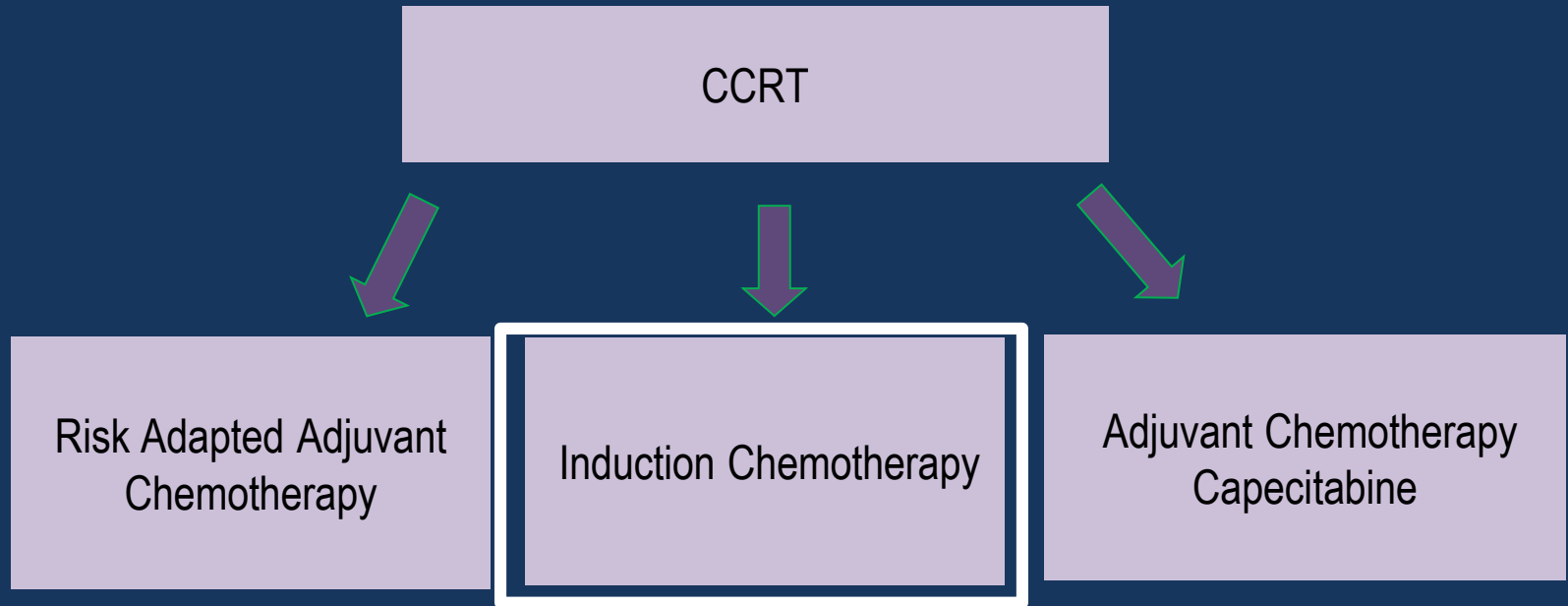
No. at risk		0	1	2	3	4	5	6	7	8
Adjuvant chemotherapy	52	35	31	30	27	23	19	14	8	8
Observation	52	40	36	32	23	22	19	14	9	9

# NRG HN001- NPC Phase II-IIIR



\*Gem 1000 m/m<sup>2</sup> d1,8 + Paclitaxel 80 mg/m<sup>2</sup> d1,8 every 21 d X 4 cycles  
87 patients enrolled

# Further progress



# NACT in Ca Nasopharynx

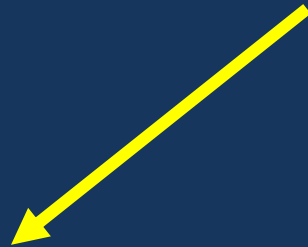
## Advantages

- Early eradication of micro metastatic disease
- Facilitate RT planning
- Better tolerated compared to adjuvant chemotherapy

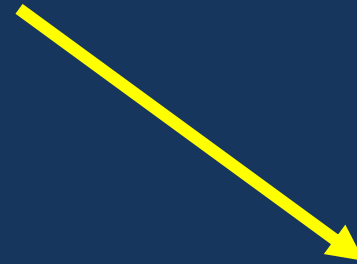
## Disadvantages

- Delay in starting the definitive treatment
- Accelerated re population
- Poor compliance to subsequent definitive Chemo RT
- Concerns regarding toxicities

# Stage III-Stage IVa Ca Nasopharynx



**Concurrent Chemo RT**



**NACT- 2-3 Cycles**



**Concurrent Chemo RT**

Chapter

# Chemotherapy in Nasopharyngeal Carcinoma

Lekha Madhavan Nair, Rejnish Ravi Kumar, Malu Rafi, Farida Nazeer, Kunnambath Ramadas and Kainickal Cessal Thommachan\*

Department of Radiation Oncology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

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Induction chemotherapy in nasopharyngeal carcinoma- A systematic review of phase III clinical trials

Farida Nazeer<sup>a, #</sup>, Jissy V. Poulose<sup>b</sup>, Cessal Thommachan Kainickal<sup>a, \*</sup>

<sup>a</sup> Department of Radiation Oncology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

<sup>b</sup> National Fellowship in Palliative Medicine (Training Program), Institute of Palliative Medicine, Calicut, Kerala, India

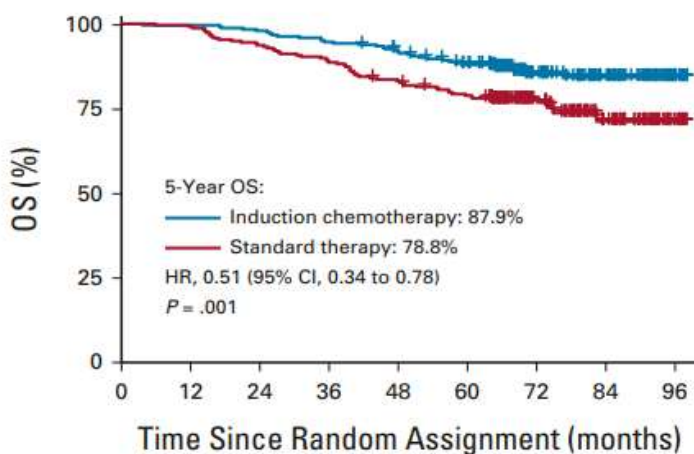
# Outcomes

Author (year)	Control	Intervention	Median follow up	DFS/FFS (Intervention vs. control arm in %)	OS	DMFS
Yang et al [22] (2019) N = 476	CCRT (cisplatin 80 mg/m <sup>2</sup> )	CDDP+5FU infusion X 2 cycles → CCRT	82.6 months	5 year DFS 73.4 vs. 63.1 P = 0.007	5 year OS 80.8 vs. 76.8 P = 0.040	5 year DMFS 82.8 vs. 73.1 P = 0.014
Li et al [24] (2019) N = 480	CCRT (Cisplatin 100 mg/m <sup>2</sup> )	Docetaxel 60 mg/m <sup>2</sup> D1, cisplatin 60 mg/m <sup>2</sup> D1, 5FU 600 mg/m <sup>2</sup> D1-5 X 3 cycles → CCRT	71.5 months	5 year FFS 77.4 vs. 66.4 P = 0.019	5 year OS 85.6 vs 77.7 P = 0.042	5 year DMFS 88 vs 79.8 P = 0.030
Zhang et al. [25] (2019) N = 480	CCRT (cisplatin 100 mg/m <sup>2</sup> )	Cisplatin 80 mg/m <sup>2</sup> D1, gemcitabine 1 g/m <sup>2</sup> D1, D8 X 3 cycles → CCRT	42.7 months	3 year Recurrence Free Survival 85.3 vs. 76.5 P = 0.001	3 year OS 94.6 vs. 90.3 HR 0.43(0.24-0.77)	3 year DMFS 91.1 VS 84.4 HR 0.43(0.25-0.73)
Frikha et al [26] (2018) N = 83	CCRT Weekly cisplatin 40 mg/m <sup>2</sup>	Docetaxel 75 mg/m <sup>2</sup> , cisplatin 75 mg/m <sup>2</sup> , 5FU 750 mg/m <sup>2</sup> D 1-5 X 3 cycles → CCRT	43.1 months	3 year PFS 73.9 vs. 57.2 P = 0.042	3 year OS 86.3 vs. 68.9 P = 0.059	3 year DMFS HR 0.53 P = 0.18
Hong et al. [27] (2018) N = 479	CCRT (cisplatin 80 mg/m <sup>2</sup> )	MEPFL regimen (mitomycin 8 mg/m <sup>2</sup> D1, Epirubicin 60 mg/m <sup>2</sup> D1, Cisplatin 60 mg/m <sup>2</sup> D1, 5FU 450 mg/m <sup>2</sup> D8. caLV 30 mg/m <sup>2</sup> D8) X3 cycles → CCRT	72 months	5 year DFS 61 vs. 50 P = 0.0264	5 year OS 72 vs. 68 P = 0.624	5 year DMFS 76 vs. 71 P = 0.28
Tan et al. [28] (2015) N = 180	CCRT (cisplatin 40 mg/m <sup>2</sup> weekly)	Paclitaxel 70 mg/m <sup>2</sup> , carboplatin AUC(2.5), Gemcitabine 1 g/m <sup>2</sup> D1, D8 X 3 cycles → CCRT	3.2 years	3 year DFS 74.9 vs. 67.4 P = 0.362	3 year OS 94.3 vs. 92.3 P = 0.494	3 year DMFS 83.8 vs. 79.9 P = 0.547

# Final Overall Survival Analysis of Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma: A Multicenter, Randomized Phase III Trial

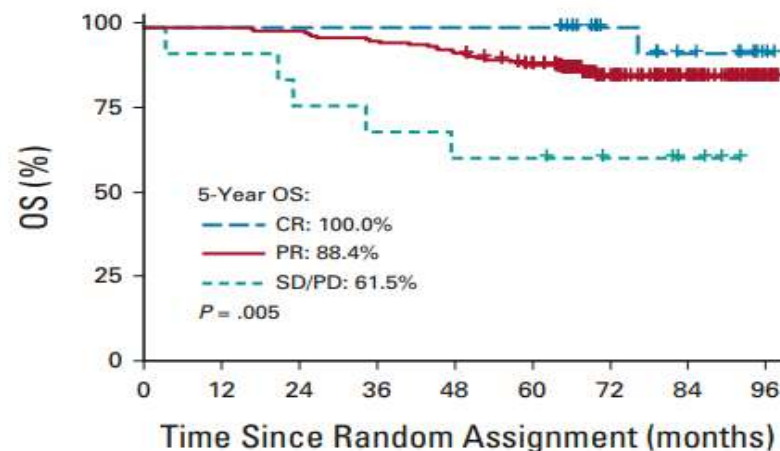
Yuan Zhang, MD, PhD<sup>1</sup>; Lei Chen, MD, PhD<sup>1</sup>; Guo-Qing Hu, MD<sup>2</sup>; Ning Zhang, MD<sup>3</sup>; Xiao-Dong Zhu, MD, PhD<sup>4</sup>; Kun-Yu Yang, MD<sup>5</sup>; Feng Jin, MD<sup>6</sup>; Mei Shi, MD, PhD<sup>7</sup>; Yu-Pei Chen, MD<sup>1</sup>; Wei-Han Hu, MD<sup>1</sup>; Zhi-Bin Cheng, MD<sup>8</sup>; Si-Yang Wang, MD<sup>9</sup>; Ye Tian, MD<sup>10</sup>; Xi-Cheng Wang, MD<sup>11</sup>; Yan Sun, MD, PhD<sup>12</sup>; Jin-Gao Li, MD<sup>13</sup>; Wen-Fei Li, MD, PhD<sup>1</sup>; Yu-Hong Li, MD<sup>14</sup>; Yan-Ping Mao, MD, PhD<sup>1</sup>; Guan-Qun Zhou, MD, PhD<sup>1</sup>; Rui Sun, MD<sup>1</sup>; Xu Liu, MD, PhD<sup>1</sup>; Rui Guo, MD, PhD<sup>1</sup>; Guo-Xian Long, MD, PhD<sup>2</sup>; Shao-Qiang Liang, MD<sup>3</sup>; Ling Li, MD, PhD<sup>4</sup>; Jing Huang, MD, PhD<sup>5</sup>; Jin-Hua Long, MD<sup>6</sup>; Jian Zang, MD<sup>7</sup>; Qiao-Dan Liu, MD, PhD<sup>9</sup>; Li Zou, MD, PhD<sup>10</sup>; Qiong-Fei Su, MD<sup>11</sup>; Bao-Min Zheng, MD, PhD<sup>12</sup>; Yun Xiao, MD<sup>13</sup>; Ying Guo, PhD<sup>15</sup>; Fei Han, MD, PhD<sup>1</sup>; Hao-Yuan Mo, MD<sup>16</sup>; Jia-Wei Lv, MD<sup>1</sup>; Xiao-Jing Du, MD, PhD<sup>1</sup>; Cheng Xu, MD, PhD<sup>1</sup>; Na Liu, MD, PhD<sup>1</sup>; Ying-Qin Li, MD, PhD<sup>1</sup>; Fang-Yun Xie, MD<sup>1</sup>; Ying Sun, MD, PhD<sup>1</sup>; Jun Ma, MD<sup>1</sup>; and Ling-Long Tang, MD, PhD<sup>1</sup>

With a median follow-up of 69.8 months



No. at risk:

Induction chemotherapy	242	241	236	228	217	202	114	69	10
Standard therapy	238	234	221	209	195	183	105	53	10



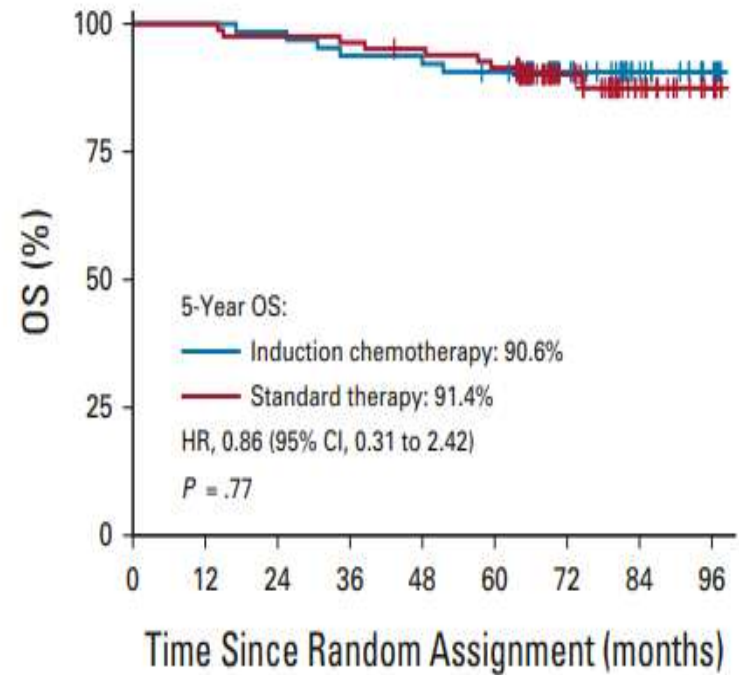
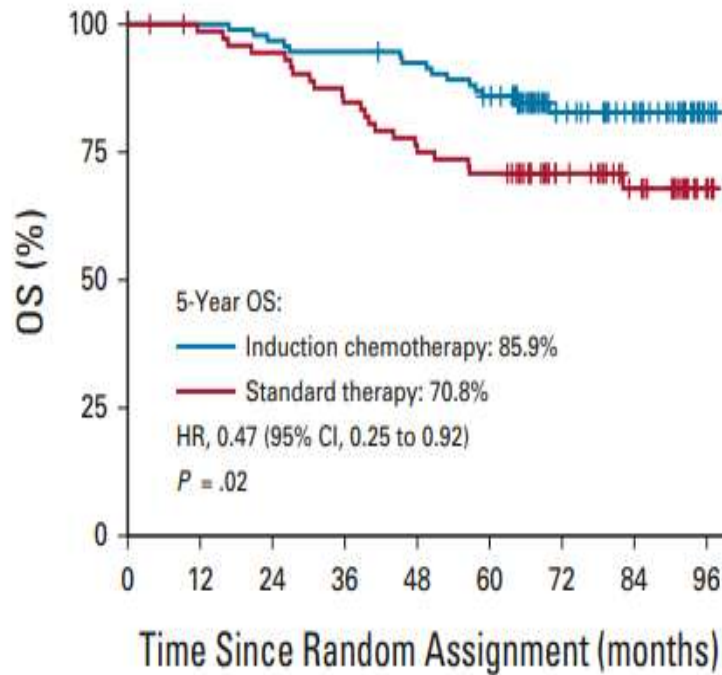
No. at risk:

CR	24	24	24	24	24	2	13	9	2
PR	202	202	199	192	182	168	93	55	8
SD/PD	13	12	10	9	8	8	6	3	0



# EBV DNA >4000

# EBV DNA <4000



No. at risk:

Induction chemotherapy	93	93	90	88	85	78	43	32	4
Standard therapy	74	71	68	61	55	51	33	22	4

No. at risk:

Induction chemotherapy	64	64	63	60	59	57	31	16	5
Standard therapy	82	82	80	79	77	74	37	17	6

Best IC regime?

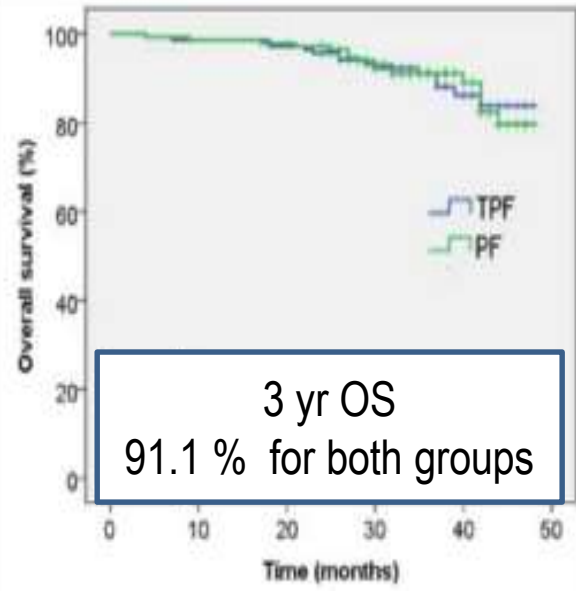
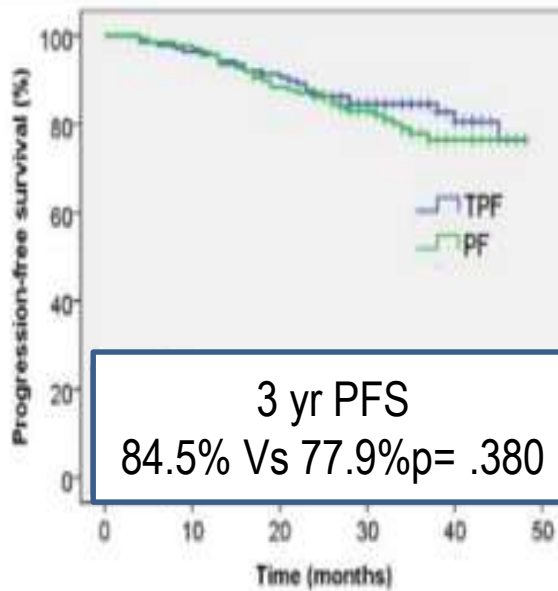
**Cisplatin and Fluorouracil Induction Chemotherapy With or Without Docetaxel in Locoregionally Advanced Nasopharyngeal Carcinoma<sup>1,2,3,4</sup>**



Ting Jin<sup>1,2,5</sup>, Wei-feng Qin<sup>1,2,5</sup>, Feng Jiang<sup>1,2</sup>, Qi-feng Jin<sup>1,2</sup>, Qi-chun Wei<sup>5</sup>, Yong-shi Jia<sup>1</sup>, Xiao-nan Sun<sup>6</sup>, Wen-feng Li<sup>7,8</sup> and Xiao-zhong Chen<sup>1,2</sup>

<sup>1</sup>Key Laboratory of Head & Neck Cancer Translational Research of Zhejiang Province, Hangzhou, Zhejiang 310022, People's Republic of China; <sup>2</sup>Department of Radiation Oncology, Zhejiang Cancer Hospital, Hangzhou, Zhejiang 310022, People's Republic of China; <sup>3</sup>Key Laboratory of Radiation Oncology in Zhejiang Province, Hangzhou, Zhejiang 310022, People's Republic of China; <sup>4</sup>Department of Radiation Oncology, Key Laboratory of Cancer Prevention and Intervention, China National Ministry of Education, The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang 310009, People's Republic of China; <sup>5</sup>Department of Radiation Oncology, Zhejiang Provincial People's Hospital, Hangzhou, Zhejiang 310014, People's Republic of China; <sup>6</sup>Department of Radiation Oncology, Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang 310000, People's Republic of China; <sup>7</sup>Department of Chemoradiation Oncology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang 325000, People's Republic of China

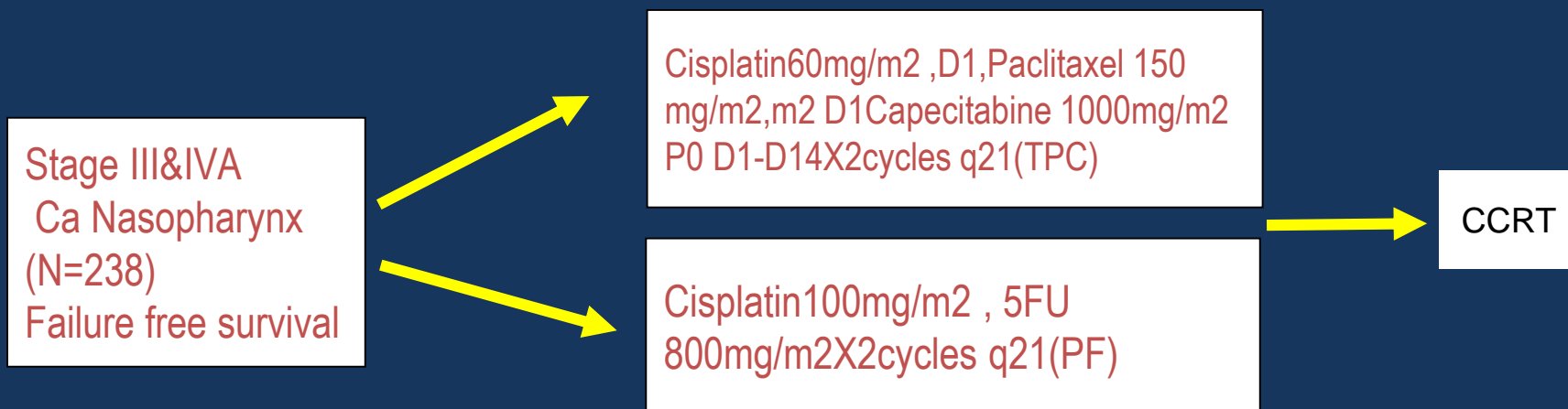
3Cycles of TPF Vs 3cycles PF  
 Non inferiority trial  
 TPF- CDDP 75 mg/M2 D1  
 Docetaxel 75/m2 D1  
 5FU 600/M2 D1-5 CI  
 PF  
 CDDP 100MG/M2 D1  
 5FU 800/M2 IV D1-5 CI  
 N= 276  
 All patients received IMRT  
 18- 70 yrs  
 Primary end point PFS



# Effect of Induction Chemotherapy With Paclitaxel, Cisplatin, and Capecitabine vs Cisplatin and Fluorouracil on Failure-Free Survival for Patients With Stage IVA to IVB Nasopharyngeal Carcinoma

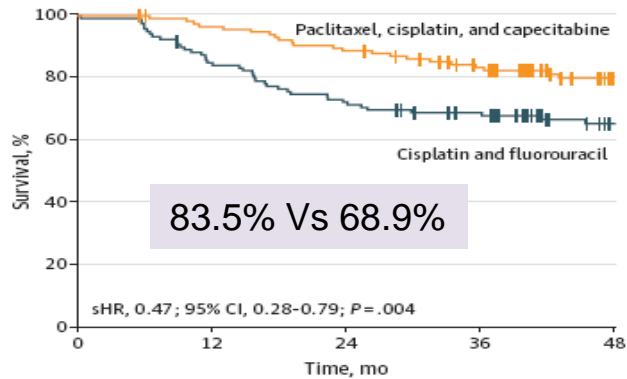
## A Multicenter Phase 3 Randomized Clinical Trial

Wang-Zhong Li, MD; Xing Lv, MD; Dan Hu, MS; Shu-Hui Lv, MS; Guo-Ying Liu, MD; Hu Liang, MD; Yan-Fang Ye, MS; Wen Yang, MD; Han-Xiong Zhang, MD; Tai-Ze Yuan, MD; De-Shen Wang, MD; Nian Lu, MD; Liang-Ru Ke, MD; Wu-Bing Tang, MD; Li-Hua Tong, MS; Zhi-Jie Chen, MS; Ting Liu, MS; Ka-Jia Cao, MD; Hao-Yuan Mo, MD; Ling Guo, MD; Chong Zhao, MD; Ming-Yuan Chen, MD; Qiu-Yan Chen, MD; Pei-Yu Huang, MD; Rui Sun, MD; Fang Qiu, MD; Dong-Hua Luo, MD; Lin Wang, MD; Yi-Jun Hua, MD; Lin-Quan Tang, MD; Chao-Nan Qian, MD; Hai-Qiang Mai, MD; Xiang Guo, MD; Yan-Qun Xiang, MD; Wei-Xiong Xia, MD



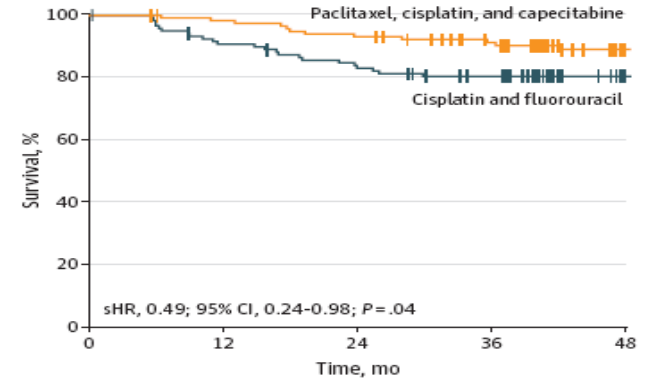
# Results- median FU 48.4 months

Failure-free survival



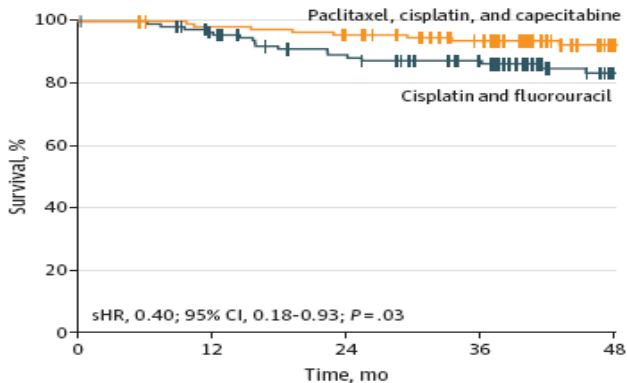
No. at risk	0	12	24	36	48
Cisplatin and fluorouracil	120	101	86	76	44
Paclitaxel, cisplatin, and capecitabine	118	112	103	89	51

Distant metastasis-free survival



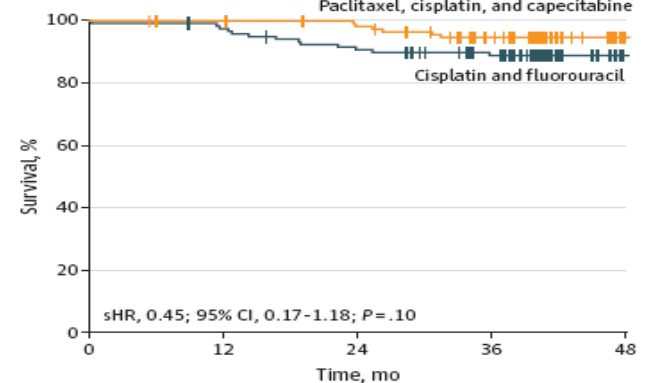
No. at risk	0	12	24	36	48
Cisplatin and fluorouracil	120	107	97	88	52
Paclitaxel, cisplatin, and capecitabine	118	114	108	96	55

Locoregional relapse-free survival



No. at risk	0	12	24	36	48
Cisplatin and fluorouracil	120	109	96	85	49
Paclitaxel, cisplatin, and capecitabine	118	114	109	95	54

Overall survival



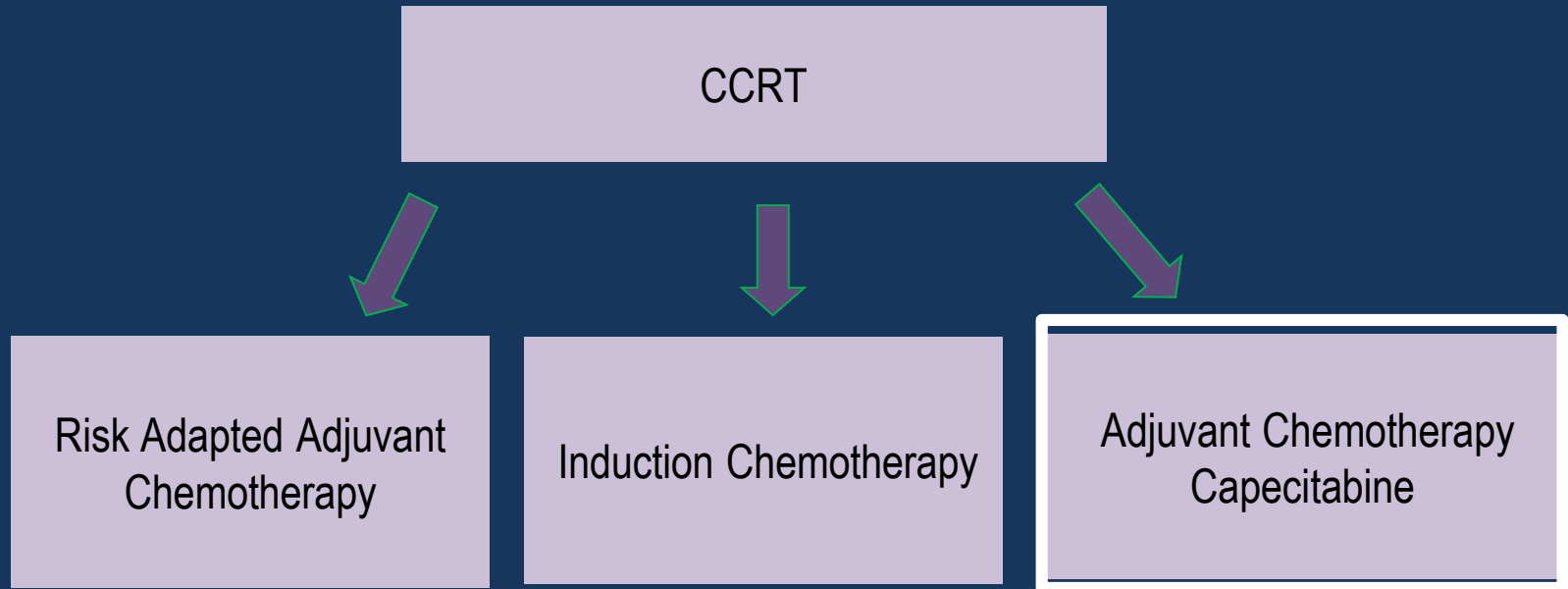
No. at risk	0	12	24	36	48
Cisplatin and fluorouracil	120	116	107	94	57
Paclitaxel, cisplatin, and capecitabine	118	116	112	97	57

# Toxicity –Similar

Adverse event	Patients, No. (%)					
	Paclitaxel, cisplatin, and capecitabine (n = 118)			Cisplatin and fluorouracil (n = 120)		
	Grade 0-1	Grade 2	Grade 3-4	Grade 0-1	Grade 2	Grade 3-4
<b>Acute hematologic toxicity</b>						
Leukopenia	60 (50.8)	40 (33.9)	18 (15.3)	65 (54.2)	28 (31.7)	17 (14.2)
Neutropenia	73 (61.9)	30 (25.4)	15 (12.7)	70 (58.3)	28 (23.3)	22 (18.3)
Anemia	68 (57.6)	37 (31.4)	13 (11.0)	70 (58.3)	39 (32.5)	11 (9.2)
Thrombocytopenia	108 (91.5)	8 (6.8)	2 (1.7)	105 (87.5)	8 (6.8)	2 (1.7)
<b>Acute nonhematologic toxicity</b>						
Dry mouth	80 (67.8)	31 (26.3)	7 (5.9)	73 (60.8)	35 (29.2)	12 (10.0)
Mucositis	53 (44.9)	32 (27.1)	33 (28.0)	48 (40.0)	38 (31.7)	34 (28.3)
Dermatitis	94 (79.7)	22 (18.6)	2 (1.7)	87 (72.5)	29 (24.2)	4 (3.3)
Diarrhea	111 (94.1)	5 (4.2)	2 (1.7)	112 (93.3)	6 (5.0)	2 (1.7)
Nausea	62 (52.5)	38 (32.2)	18 (15.3)	63 (52.5)	32 (26.7)	25 (20.8)
Vomiting	71 (60.2)	25 (21.2)	22 (18.6)	66 (55.0)	35 (29.2)	19 (15.8)
Hepatotoxicity	96 (81.4)	19 (16.1)	3 (2.5)	101 (84.2)	16 (13.3)	3 (2.5)
Nephrotoxicity <sup>a</sup>	112 (94.9)	6 (5.1)	0	112 (93.3)	7 (5.8)	1 (0.8)
Hand-foot syndrome	116 (98.3)	2 (1.7)	0	119 (99.2)	1 (0.8)	0
Allergic reaction	112 (94.9)	5 (4.2)	1 (0.8)	117 (97.5)	3 (2.5)	0
Weight loss	91 (77.1)	25 (21.2)	2 (1.7)	90 (75.0)	27 (22.5)	3 (2.5)

3 drug NACT is not superior to 2 drug

# Further progress





# Adjuvant Chemotherapy

**Stage III-Stage IVa  
Ca Nasopharynx**

**CCRT+/-IC**

**CCRT**

**Adjuvant Capecitabine**



# Metronomic capecitabine as adjuvant therapy in locoregionally advanced nasopharyngeal carcinoma: a multicentre, open-label, parallel-group, randomised, controlled, phase 3 trial

Yu-Pei Chen\*, Xu Liu\*, Qin Zhou\*, Kun-Yu Yang\*, Feng Jin\*, Xiao-Dong Zhu\*, Mei Shi\*, Guo-Qing Hu\*, Wei-Han Hu\*, Yan Sun, Hong-Fen Wu, Hui Wu, Qin Lin, Hui Wang, Ye Tian, Ning Zhang, Xi-Cheng Wang, Liang-Fang Shen, Zheng-Zheng Liu, Jing Huang, Xiu-Ling Luo, Ling Li, Jian Zang, Qi Mei, Bao-Min Zheng, Dan Yue, Jing Xu, San-Gang Wu, Yan-Xia Shi, Yan-Ping Mao, Lei Chen, Wen-Fei Li, Guan-Qun Zhou, Rui Sun, Rui Guo, Yuan Zhang, Cheng Xu, Jia-Wei Lv, Ying Guo, Hui-Xia Feng, Ling-Long Tang†, Fang-Yun Xie†, Ying Sun†, Jun Ma†

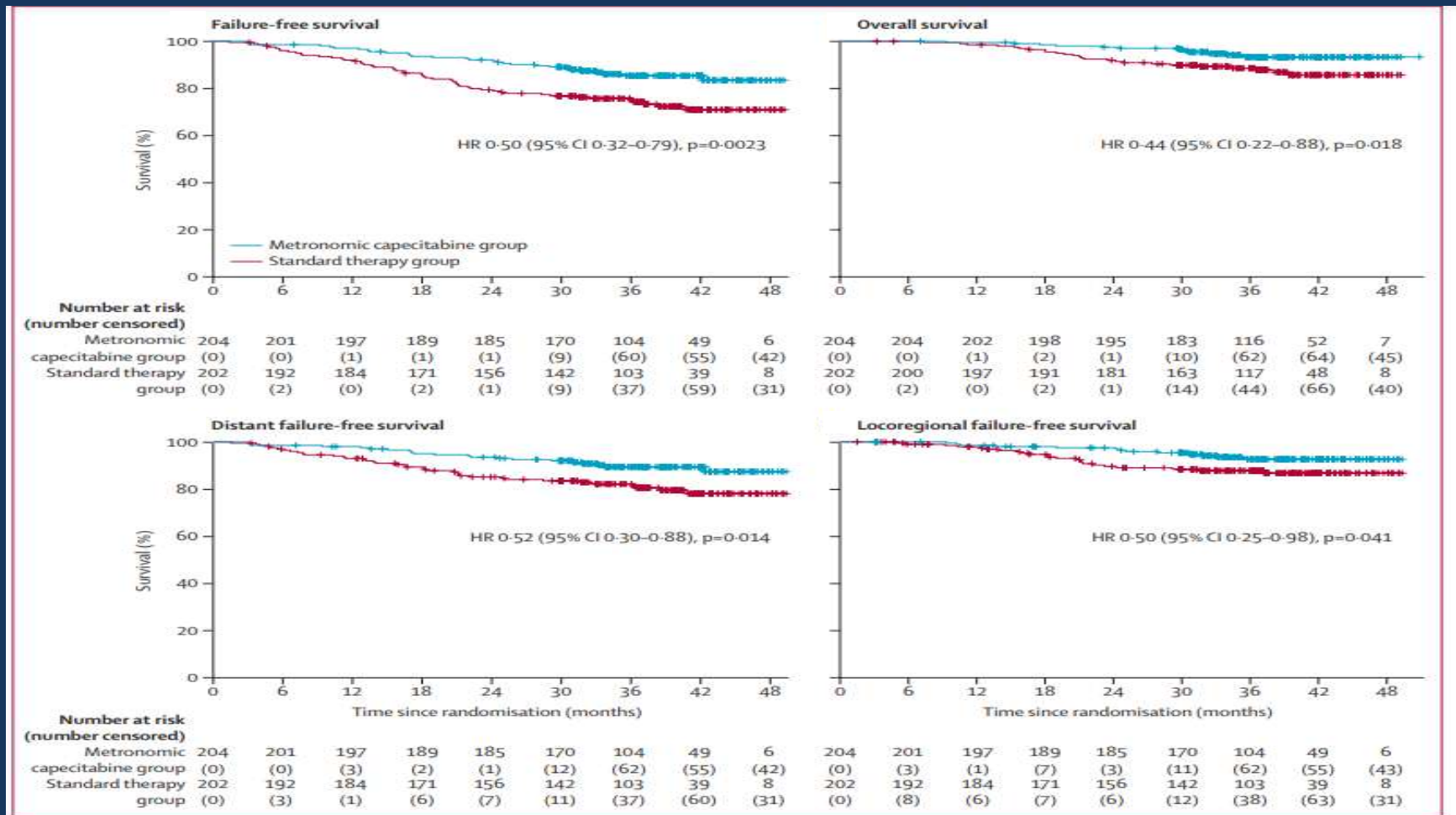
- Stage III–IVA, excluding T3–4N0 and T3N1 disease
- FFS
- N=406
- Standard therapy

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E

Capecitabine 650 mg/m<sup>2</sup> body surface area twice daily for 1 year

Observation

# Results- Median follow up-38 months



# Toxicity

	Metronomic capecitabine group (n=201)			Standard therapy group (n=200)		
	Any grade	Grade 1 or 2	Grade 3 or 4	Any grade	Grade 1 or 2	Grade 3 or 4
Any adverse event	182 (91%)	147 (73%)	35 (17%)	112 (56%)	101 (51%)	11 (6%)
Haematological adverse event						
Leukopenia	54 (27%)	48 (24%)	6 (3%)	39 (20%)	33 (17%)	6 (3%)
Neutropenia	37 (18%)	30 (15%)	7 (3%)*	25 (13%)	20 (10%)	5 (3%)
Anaemia	71 (35%)	70 (35%)	1 (<1%)	51 (26%)	49 (25%)	2 (1%)
Thrombocytopenia	24 (12%)	23 (11%)	1 (<1%)	19 (10%)	19 (10%)	0
Non-haematological adverse event						
Hand-foot syndrome	117 (58%)	<u>99 (49%)</u>	<u>18 (9%)</u>	0	0	0
Fatigue	55 (27%)	54 (27%)	1 (<1%)	36 (18%)	36 (18%)	0
Nausea	44 (22%)	42 (21%)	2 (1%)	21 (11%)	21 (11%)	0
Sensory neuropathy	37 (18%)	34 (17%)	3 (1%)	16 (8%)	14 (7%)	2 (1%)
Anorexia	36 (18%)	36 (18%)	0	18 (9%)	18 (9%)	0
Weight loss	27 (13%)	30 (15%)	0	13 (7%)	13 (7%)	0
Vomiting	26 (13%)	25 (12%)	1 (<1%)	14 (7%)	14 (7%)	0
Elevated ALT or AST concentrations	23 (11%)	23 (11%)	0	15 (8%)	15 (8%)	0
Mucositis or stomatitis	21 (10%)	<u>20 (10%)</u>	1 (<1%)	9 (5%)	9 (5%)	0
Diarrhoea	19 (9%)	<u>18 (9%)</u>	1 (<1%)	4 (2%)	4 (2%)	0

Research

JAMA Oncology | **Original Investigation**

# Adjuvant Capecitabine Following Concurrent Chemoradiotherapy in Locoregionally Advanced Nasopharyngeal Carcinoma A Randomized Clinical Trial

Jingjing Miao, MD; Lin Wang, MD; Sze Huey Tan, PhD; Jin-gao Li, MD; Junlin Yi, MD; Enya H.W. Ong, BSc; Laura L.Y. Tan, MBBS; Ye Zhang, MD; Xiaochang Gong, MD; Qiuyan Chen, MD; Yan-qun Xiang, MD; Ming-yuan Chen, MD; Ying Guo, MS; Xing Lv, MD; Wei-xiong Xia, MD; Linqun Tang, PhD; Xiaowu Deng, PhD; Xiang Guo, PhD; Fei Han, MD; Hai-qiang Mai, MD; Melvin L. K. Chua, PhD; Chong Zhao, PhD

- T3-4N2 or T1-4N3
- Pre-treatment plasma EBV DNA >20,000 copy/ml
- GTVnx of >30 cm<sup>3</sup>
- SUVmax of >10.0 by <sup>18</sup>FDG PET-CT in primary or node, with any larger than 4 cm
- FFS
- N=180

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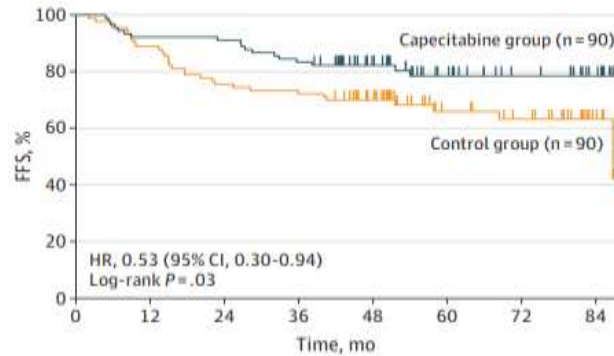
Capecitabine 1 gm/m<sup>2</sup> BID D1-D14 q3weeks X8 cycles

Observation

JAMA Oncol. doi:10.1001/jamaoncol.2022.4656

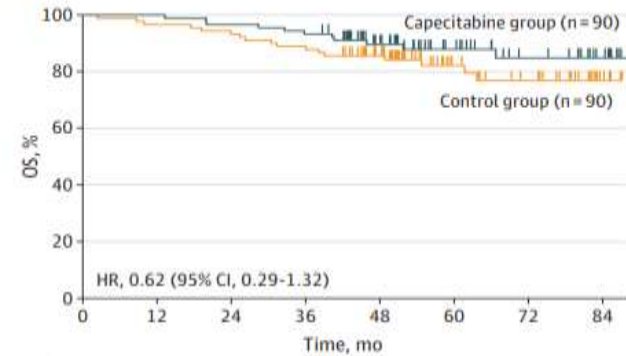
# Median follow up of 58 months

Failure-free survival



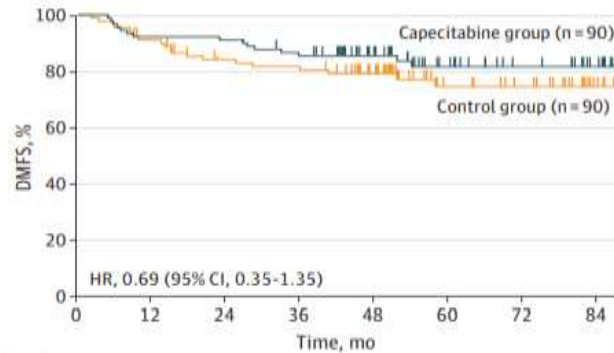
No. at risk (censored)		0	12	24	36	48	60	72	84
Capecitabine group	90/0	83/0	82/0	75/0	53/21	33/39	23/49	13/59	
Control group	90/0	80/0	68/0	65/0	52/11	26/35	21/39	6/54	

Overall survival



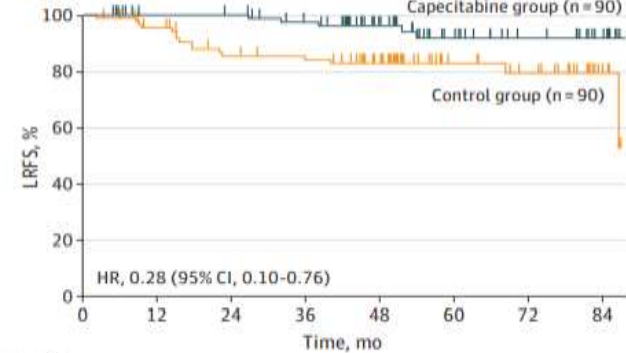
No. at risk (censored)		0	12	24	36	48	60	72	84
Capecitabine group	90/0	90/0	87/6	84/0	59/22	37/43	25/54	14/65	
Control group	90/0	87/0	84/0	79/0	64/13	32/43	24/49	7/66	

Distant metastasis-free survival



No. at risk (censored)		0	12	24	36	48	60	72	84
Capecitabine group	90/0	83/0	82/0	75/2	53/24	33/42	23/52	13/62	
Control group	90/0	80/2	68/8	65/8	52/20	26/44	21/49	6/64	

Locoregional relapse-free survival



No. at risk (censored)		0	12	24	36	48	60	72	84
Capecitabine group	90/0	83/7	82/8	75/13	53/34	33/51	23/62	13/72	
Control group	90/0	80/6	68/10	65/2	52/24	26/50	21/54	6/69	

# Acute Toxicity

- G3-4 acute toxicity (57.8% vs 51.1%)
- Hand foot syndrome (3.5% vs 0%)
- Xerostomia (11.1% vs 3.3%)
- Mucositis (23.3% vs 16.7%)
- Anemia (5.6% vs 2.2%)

# Adjuvant Capecitabine after CCRT

- Difference in inclusion criteria
- Difference in dose and duration
- Number of patients were less in the second study
- NACT permitted in one study
- 2 studies – OS Survival benefit
- Increased toxicity
- Awaiting long term follow up
- Adjuvant in patients received NACT?





Contents lists available at ScienceDirect

# Clinical and Translational Radiation Oncology

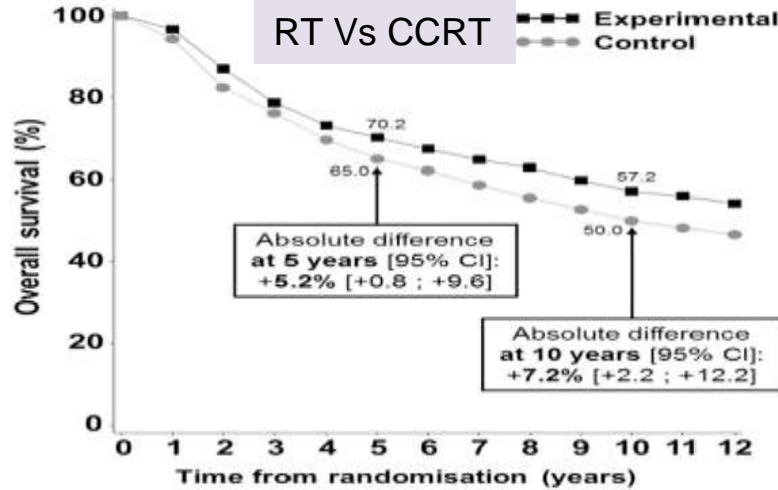
journal homepage: [www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology](http://www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology)



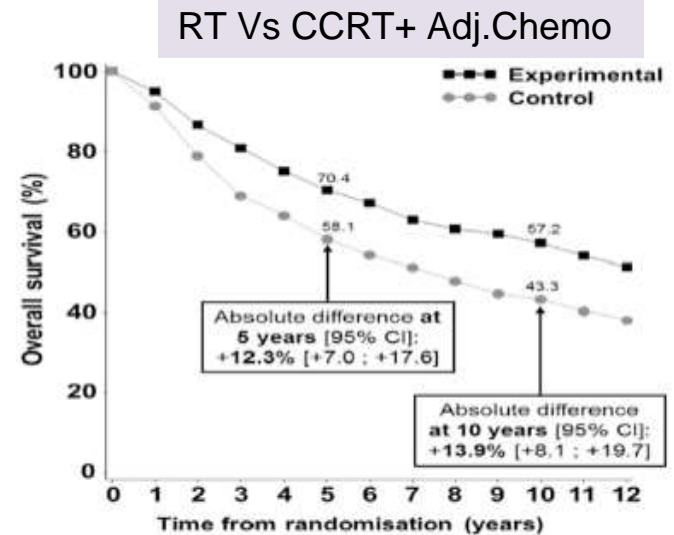
Original Research Article

## Meta-analysis of chemotherapy in nasopharynx carcinoma (MAC-NPC): An update on 26 trials and 7080 patients

Pierre Blanchard<sup>a,b,\*</sup>, Anne W.M. Lee<sup>c</sup>, Alexandra Carmel<sup>b,d</sup>, Ng Wai Tong<sup>c</sup>, Jun Ma<sup>e</sup>, Anthony T.C. Chan<sup>f</sup>, Ruey Long Hong<sup>g</sup>, Ming-Yuan Chen<sup>h</sup>, Lei Chen<sup>h</sup>, Wen-Fei Li<sup>h</sup>, Pei-Yu Huang<sup>h</sup>, Dora L.W. Kwong<sup>i</sup>, Sharon S.X. Poh<sup>j</sup>, Roger Ngan<sup>c</sup>, Hai-Qiang Mai<sup>h</sup>, Camille Ollivier<sup>b,d</sup>, George Fountzilas<sup>k</sup>, Li Zhang<sup>h</sup>, Jean Bourhis<sup>l</sup>, Anne Aupérin<sup>b,d</sup>, Benjamin Lacas<sup>b,d</sup>, Jean-Pierre Pignon<sup>b,d</sup>, on behalf of the MAC-NPC collaborative Group



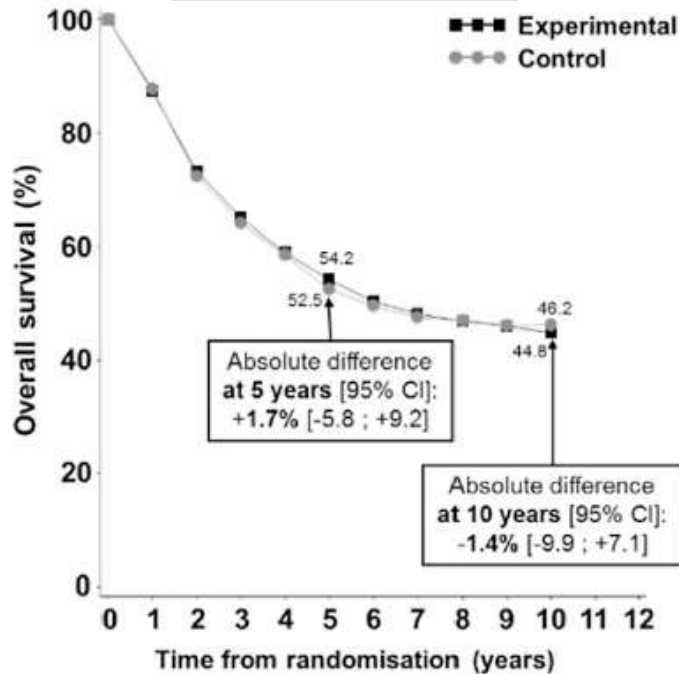
	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
Experimental	116 / 1714	146 / 1974	90 / 2244	34 / 1147
Control	157 / 1655	146 / 1847	106 / 1979	33 / 934



	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
Experimental	84 / 1188	102 / 1458	68 / 1537	70 / 1259
Control	135 / 1151	129 / 1231	74 / 1221	55 / 916

# Efficacy

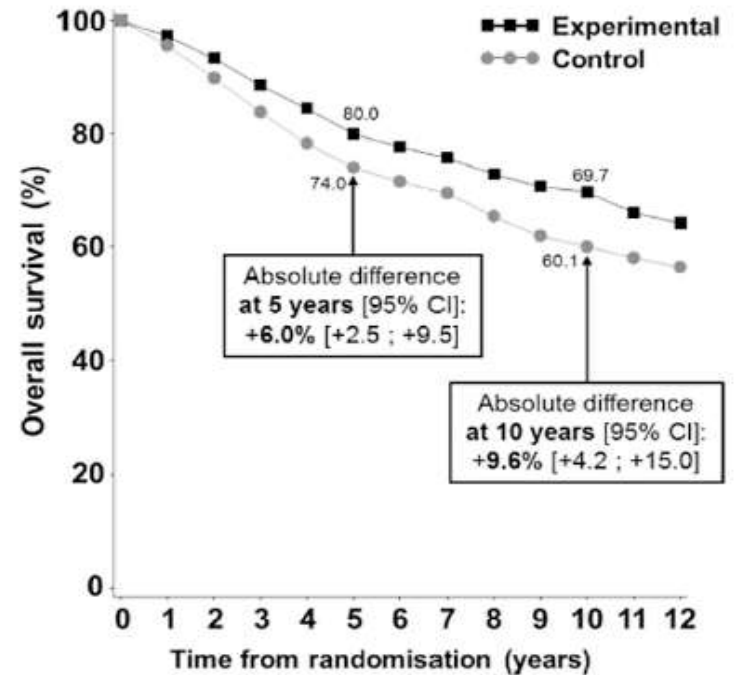
## RT Vs NACT+RT



Number of deaths / person-years

	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
Experimental	102 / 664	61 / 599	17 / 383	0 / 36
Control	107 / 675	61 / 563	13 / 386	0 / 49

## CCRT Vs NACT+CCRT




Number of deaths / person-years

	Years [0;2[	Years [2;5[	Years [5;10[	Years 10+
Experimental	80 / 2308	139 / 2718	48 / 1658	8 / 207
Control	119 / 2246	169 / 2558	63 / 1579	7 / 221

*Research Article*

## Clinical Profile and Treatment Outcomes in Patients Treated with Intensity-Modulated Radiotherapy (IMRT) for Carcinoma Nasopharynx: A Retrospective Analysis

Farida Nazeer,<sup>1</sup> R. Rejnish Kumar,<sup>1</sup> Malu Rafi,<sup>1</sup> Tapesh Bhattacharya,<sup>1</sup>  
Aparna Mullangath Prakasan,<sup>1</sup> Kumar P. Naveen,<sup>1</sup> Preethi George,<sup>2</sup>  
Ramadas Kunnambath,<sup>1</sup> and Kainickal Cessal Thommachan <sup>1</sup>

<sup>1</sup>Department of Radiation Oncology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

<sup>2</sup>Department of Cancer Epidemiology and Biostatistics, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

Correspondence should be addressed to Kainickal Cessal Thommachan; [drcessalthomas@gmail.com](mailto:drcessalthomas@gmail.com)

Chemotherapy sequencing	N=84	No. of patients (%)
Neoadjuvant chemotherapy alone		5 (6.3%)
Neoadjuvant + concurrent		34 (41.9%)
Concurrent + adjuvant		4 (4.9%)
Neoadjuvant + concurrent + adjuvant		3 (3.7%)
Concurrent alone		28 (34.5%)
No chemotherapy		7 (8.7%)

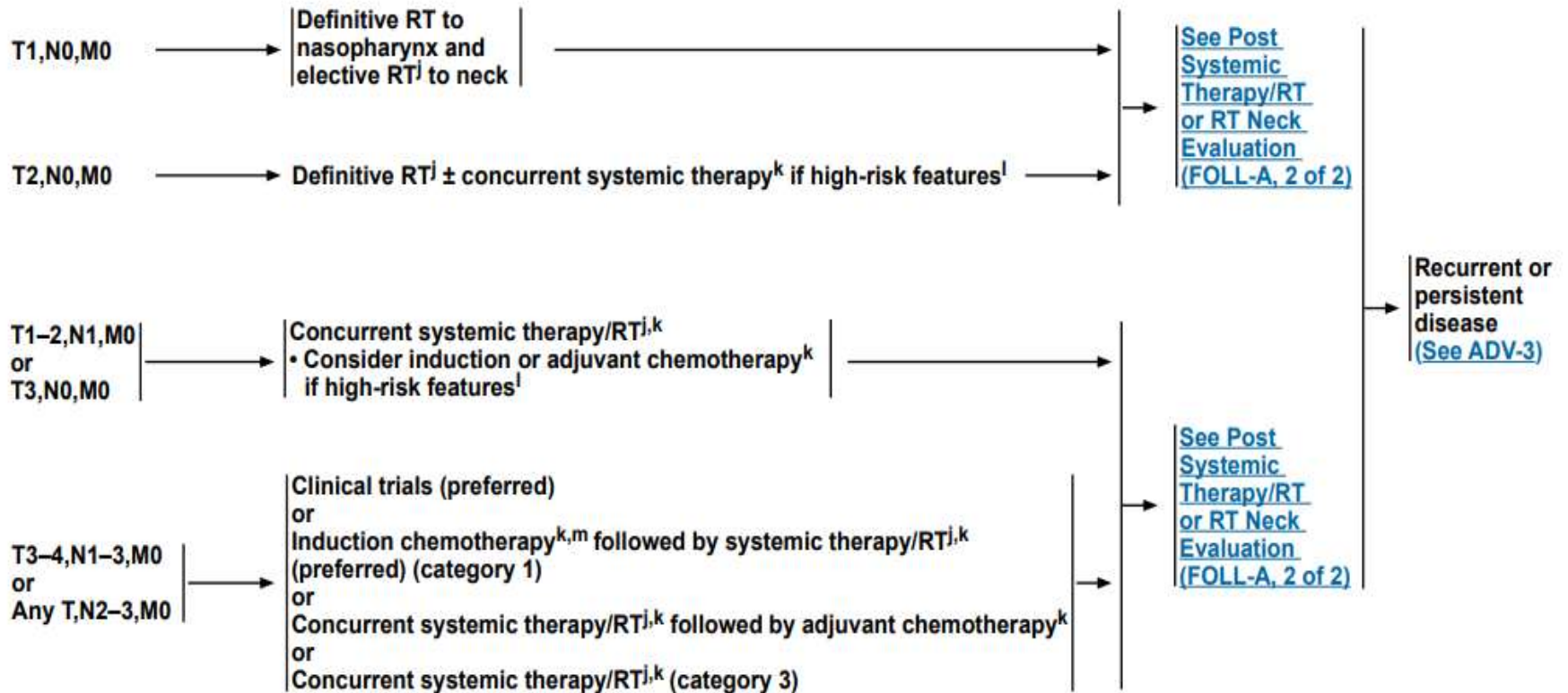
Stage ( <i>n</i> = no. of patients)	Survival probability (%)
I ( <i>n</i> = 2)	100
II ( <i>n</i> = 19)	67.0
III ( <i>n</i> = 31)	70.4
IV ( <i>n</i> = 29)	68.1



### CLINICAL STAGING

### TREATMENT OF PRIMARY AND NECK<sup>i</sup>

### FOLLOW-UP



# Conclusions

- Stage I- Radical RT
- UNI in N0- same efficacy with less late toxicity
- Stage II – No role for NACT
- Stage II- ???IMRT alone
- Stage III& IVa – IC followed by CCRT
- Weekly CDDP = 3 Weekly with increased toxicity
- Superiority of 3 drug NACT is not proven
- Adjuvant Capecitabine - Promising results with excess toxicity
- Adjuvant CDDP+5FU in risk adapted approach – No benefit

# Thank you



[drcessalthomas@gmail.com](mailto:drcessalthomas@gmail.com)