

Practice Guidelines for Breast Cancer Treatment in China

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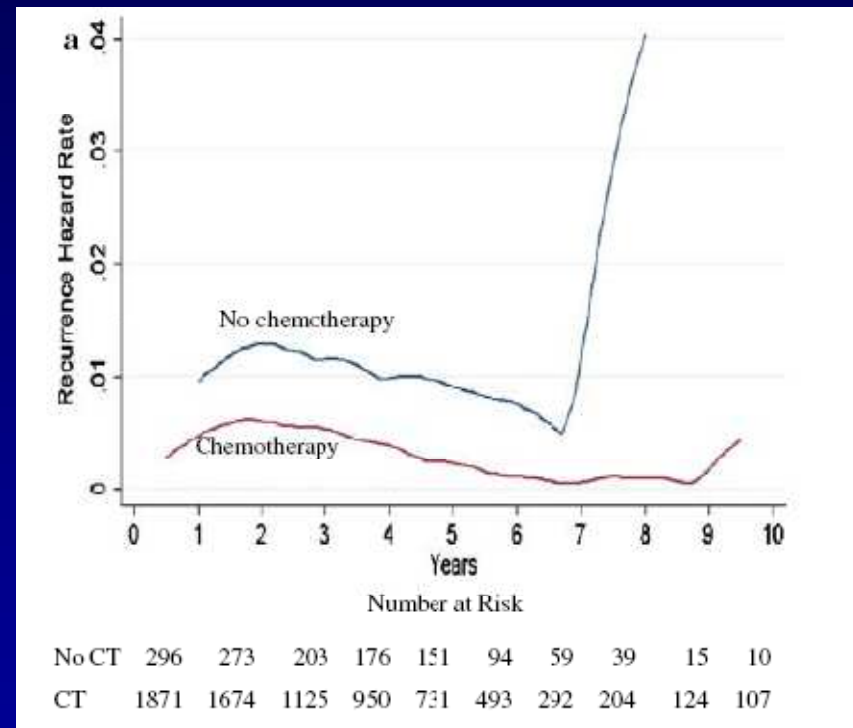
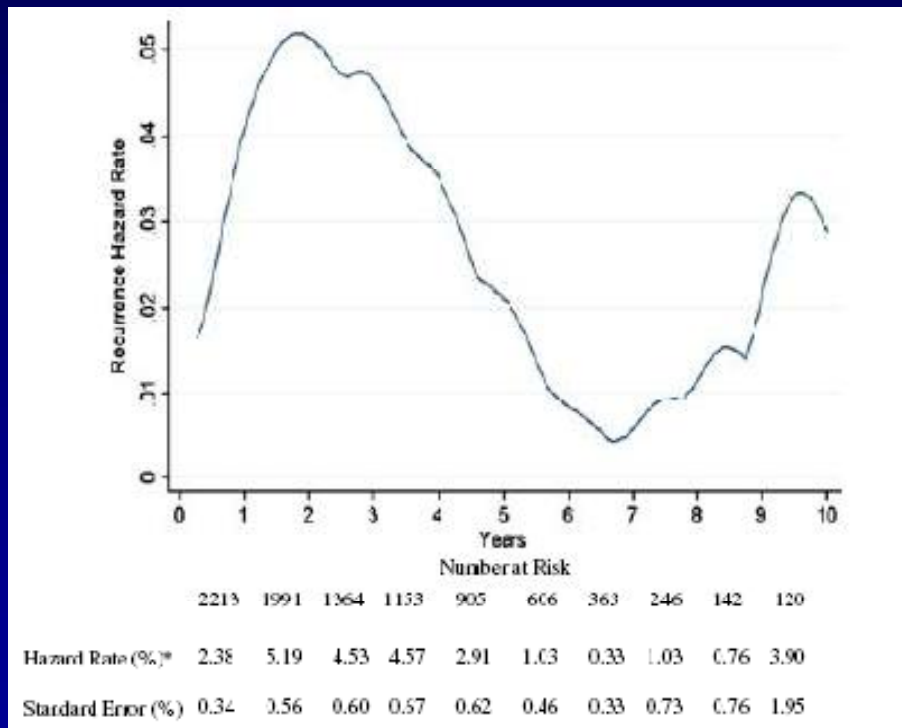
Overview of Breast Cancer Incidence in China

- China has 15% of global burden of breast cancer
 - **Approximately 190,000** new cases annually¹
- The incidence of breast cancer is increasing and expected to surpass other types of cancer in the next decade
 - **Near forty percent increase in 5 years (2000-2005)** ¹
 - **Top 1 cancer in women in more than ten large cities** ²

1. Estimates of Cancer Incidence in China for 2000 and Projections for 2005, Yang L, et al.

2. An annual report: Cancer Incidence in 35 Cancer Registries in China, 2003, Zhang SW, et.al.

Hazard rate of recurrence following surgery in 2,213 Chinese patients



- 2 major peaks of recurrence: within 2 years after surgery, and on 9th year
- Adjuvant chemo may pose long-lasting survival effect on survival

Characteristics of Breast Cancer in Chinese patients

- Higher percentage of young patients than in Western countries
 - *50% of patients are premenopausal*
- Higher percentage of ER negative patients than in Western countries
 - *40%-50% are ER negative*
- Two major peaks of recurrence

1. Yao S, Xu B, et al. Ana Oncol, 2009, 20(2): 387-9. 2. Fan L et al., Breast cancer Res Treat. 2009. 2.
3. Chow,LW. J surg oncol 2000;75:172-5 . 4.. Yu, et al. World J. Surg. 2005 29(7):(813-818.
5. Chu KC et al . Cancer 2001 92(1):37-45. 6. Stierer. Ann Surg. 1993 Jul;218(1):13-21. 7. Yin w, et al.
Breast Ca Res Treat. 2009 ; 114: 527-535

Practice Guidelines for Breast Cancer in China

- NCCN guideline in Chinese edition
- Chinese Society of Breast Cancer (CSBC)

Guideline

cNCCN and CSBC Practice Guidelines in Breast Cancer

- Work-up/initial evaluation
- Locoregional treatment
- Adjuvant / neoadjuvant systemic treatment
- Surveillance / follow-up
- Evaluation of recurrence
- Treatment of recurrence /metastatic disease

Treatment of Breast Cancer

cNCCN and CSBC Guidelines: Adjuvant Chemotherapy

- Tumor size >1 cm

Tubular and colloid: ≥ 3 cm with ER or PR positive:
adjuvant endocrine therapy; ER negative and PR
negative: chemotherapy

- Lymph node metastasis
- Treatment should be individualized for those
over 70 y old

cNCCN and CSBC Guidelines: Adjuvant Endocrine Therapy

- Premenopausal: Tamoxifen \pm ovarian suppression or ablation
- Postmenopausal: Aromatase inhibitors (upfront or sequential)

Comparison of results in Interim Analysis between Global and China — **Efficacy**

Efficacy	HERA-Global	HERA-China
2 year's DFS	Absolute difference: 7.6%	Absolute difference: 8.5%
2 year's RFS	RR 0.51	RR 0.1
2 year's DDFS	RR 0.50	RR 0.11
2 year's OS	NS	NS

Comparison of results in Interim Analysis between Global and China — Safety

	HERA-Global		HERA-China	
	Control	Treatment	Control	treatment
At least one AE	46%	70%	13%	40%
SAE	5%	8%	2%	4%
Common treatment-related AE	Related with Herceptin infusion (Headache, chill, fever and nausea)		Most related with Herceptin infusion (Fever, weakness, headache, and arthralgia)	
New safety issue	Not found		Not found	

Comparison of results in Interim Analysis between Global and China — **Cardiotoxicity**

	HERA-Global		HERA-China	
	Control	Treatment		
Death	1 pts	-	-	-
NYHA stage III CHF	-	8 pts	-	-
NYHA stage IV CHF	-	2 pts	-	-
Second heart endpoint	0.5%	3%	-	-
LVEF ↓			LVEF ↓50% in 1 pt	

Conclusion: Interim Analysis in Chinese Patients

- One year Herceptin adjuvant therapy can improve DFS, RFS and DDFS in Chinese EBC patients
- Favorable tolerance, no new or unanticipated toxicity

cNCCN and CSBC Guidelines: Adjuvant Trastuzumab Treatment

- Regimens
 - AC → PH/DH
 - DCH (Docetaxel, carboplatin, trastuzumab)
 - Chemotherapy → H
- Trastuzumab should be given for one year

Monitoring for Cardiac Function

LVEF monitoring every 4~6 months

LVEF < 50%

Suspend trastuzumab treatment, watch or alleviate symptoms

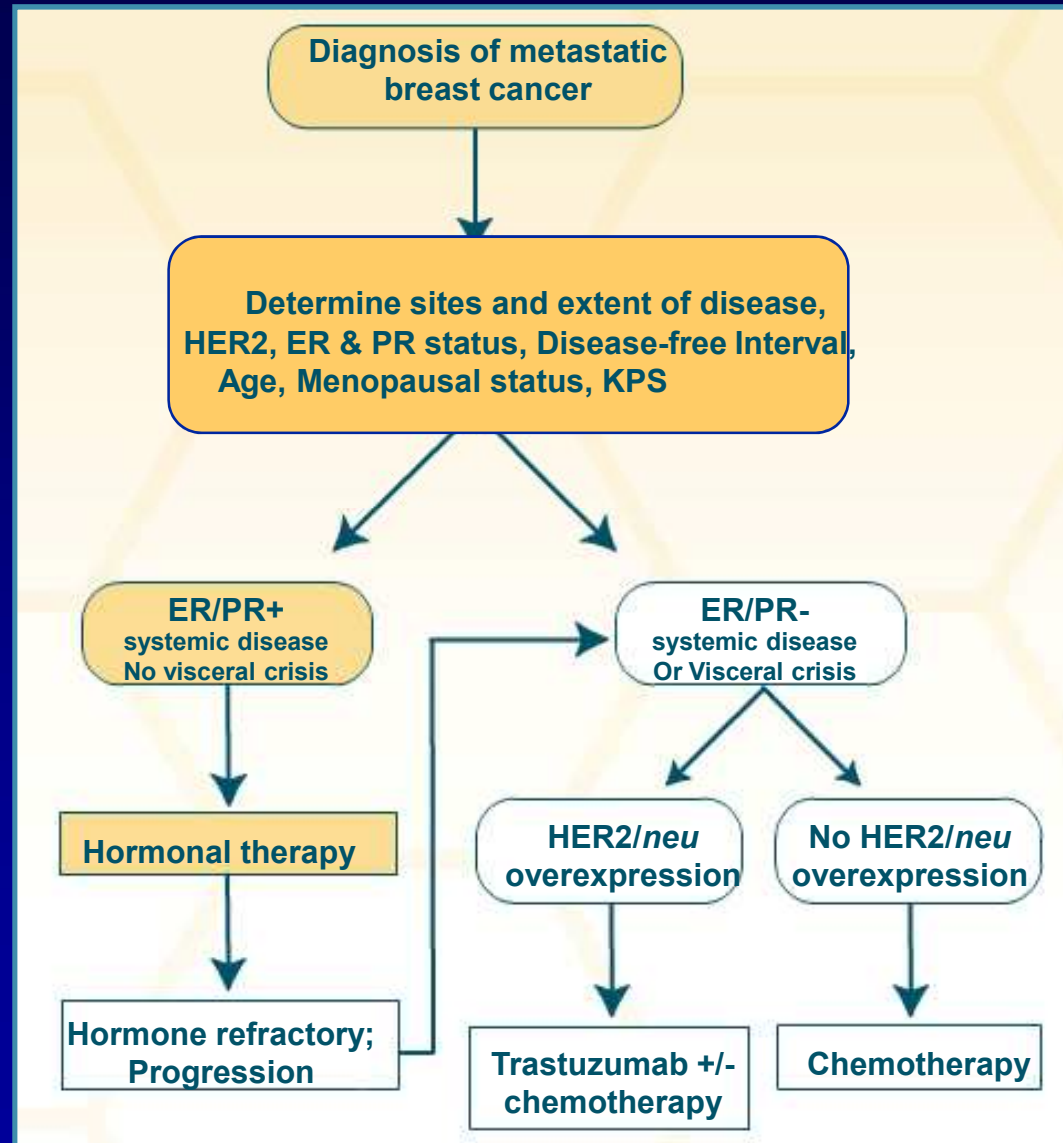
Return to over 50%

Deteriorate

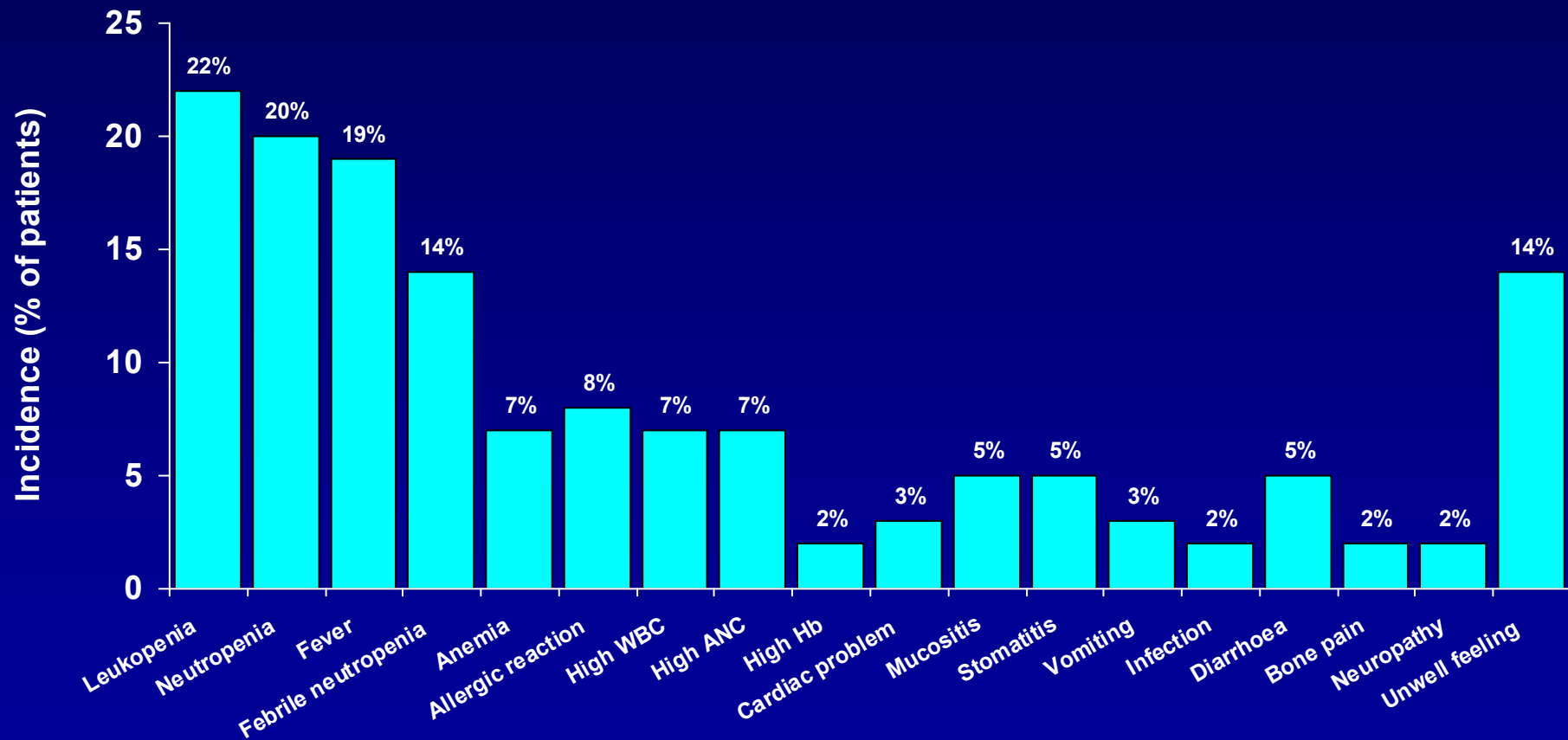
Continue treatment

Stop trastuzumab treatment

Management of Metastatic Breast Cancer



Clinical Experience With Docetaxel for Chinese Breast Cancer Patients: Hematologic Toxicity Profiles

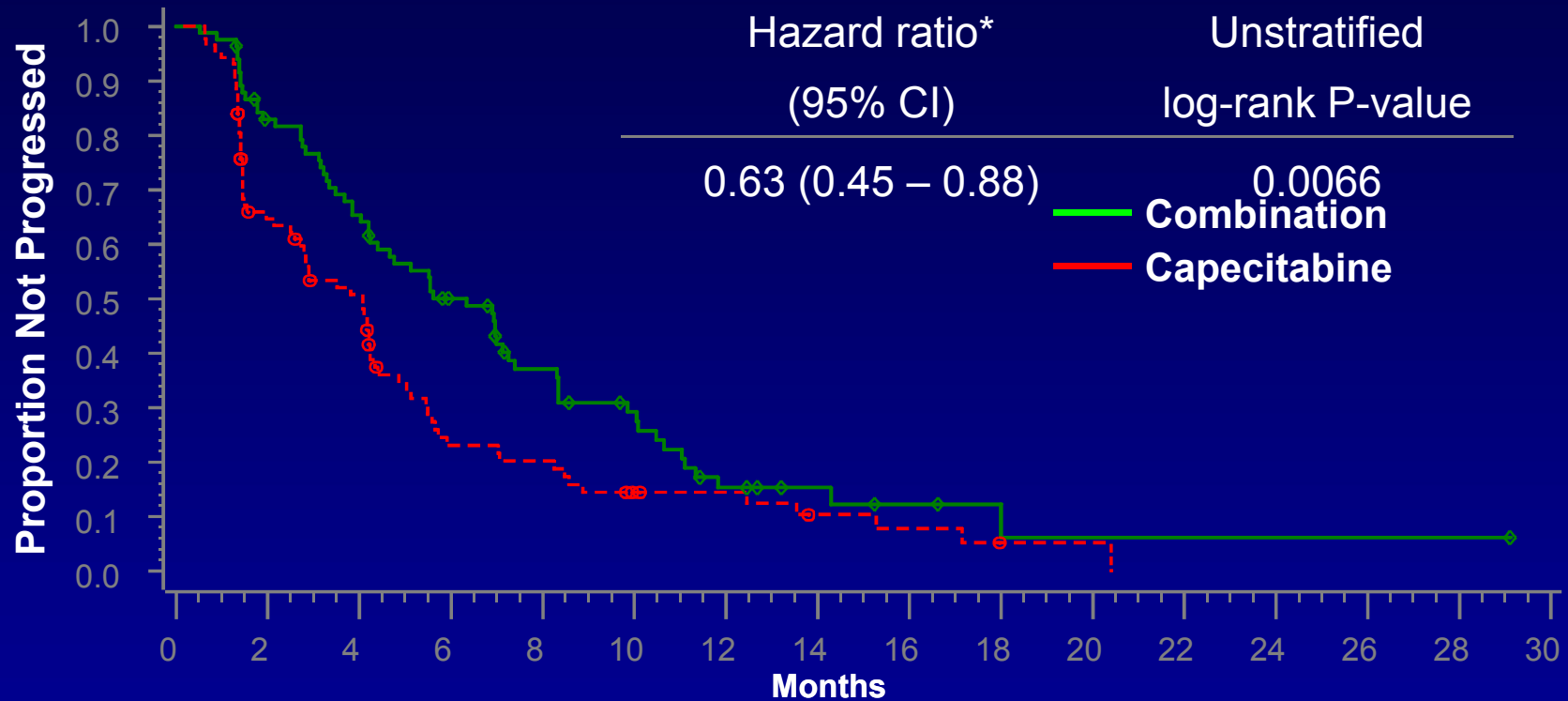


CA163046 Objective Response

Efficacy Parameter	Combination N = 375		Capecitabine N = 377	
	Asian N = 83	Non-Asian N = 292	Asian N = 87	Non-Asian N = 290
IRRC ORR, n (%)	29 (35)	101 (35)	8 (9)	46 (16)
Median duration of response, months (95% CI)	6.9 (5.6 - 7.1)	6.4 (5.5 - 8.1)	4.2 (3.0 - 16.3)	5.8 (4.2 - 8.6)

Source: Reference 4; ORR = objective response rate; MBC = metastatic breast cancer

CA163046 Progression Free Survival - ASIANS



	# Progressed / # Randomized	Median (95% CI)
Combination	64 / 83	6.3 (4.2 – 7.3)
Capecitabine	72 / 87	4.1 (2.7 – 4.2)

Source: Reference [5]; PFS = progression-free survival

CA163046 Treatment-related Non-hematologic AEs

Grade 3/4 Related Adverse Events	Number (%) of Patients	
	Combination N = 369	
	Asian N = 80	Non-Asian N = 289
Any	57 (71)	195 (67)
Peripheral sensory neuropathy	16 (20)	62 (21)
Myalgia	12 (15)	17 (6)
Hand and foot syndrome	9 (11)	58 (20)
Fatigue	6 (8)	27 (9)
Arthralgia	4 (5)	6 (2)
Stomatitis	3 (4)	3 (1)
Diarrhea	2 (3)	19 (7)
Asthenia	0	27 (9)
Related SAEs	24 (30)	67 (23)
Related AEs leading to discontinuation	31 (39)	105 (36)

Source: Reference 4; MedDRA = Medical Dictionary for Drug Regulatory Affairs
 aBy MedDRA preferred terms. Peripheral sensory neuropathy is reported as a composite of MedDRA preferred terms.

CA163046 Grade 3/4 Hematologic Abnormalities

Hematology parameter ^a	Number (%) of Patients			
	Combination N = 369			
	Asian N = 80		Non-Asian N = 289	
	Grade 3	Grade 4	Grade 3	Grade 4
Neutropenia	21 (26)	41 (51)	95 (33)	92 (32)
Anemia	8 (10)	2 (3)	20 (7)	5 (2)
Thrombocytopenia	6 (8)	5 (6)	12 (4)	7 (2)

Source: Reference 4

^aBased on laboratory values for absolute neutrophil count (ANC), hemoglobin, and platelets (Common Terminology Criteria [CTC] version 3.0)

cNCCN and CSBC Guidelines in MBC: Chemotherapy

First Line Chemotherapy

- Sequential use of single agents and combination chemotherapy: Both regimens are active for MBC
 - Sequential single agent chemotherapy may be used in patients with symptomless, few sites of metastases, and no metastasis at vitals: Prior to tolerance and QOL.
 - Combination chemotherapy refer to diffuse metastatic disease and symptomatic patients. Primary objectives of treatment are tumor cytoreduction and symptom control

cNCCN and CSBC Guidelines: Chemotherapy in MBC

● Combination

- Anthracycline combinations
- Docetaxel and Capecitabine or Bevacizumab
- Paclitaxel + Gemcitabine or Carboplatin or Bevacizumab
- Ixabepilone + Capecitabine

● Single agents

- Paclitaxel qw or Docetaxel q 3w
- Capecitabine
- Ixabepilone
- Vinorelbine and others

cNCCN and CSBC Guidelines: Hormone Therapy in MBC

- **Postmenopausal**

- Aromatase inhibitors favored as 1st-line
- No difference in outcome of exemestane vs fulvestrant after disease progression to non-steroidal AI

- **Premenopausal**

- LH-RH agonists
- Tamoxifen

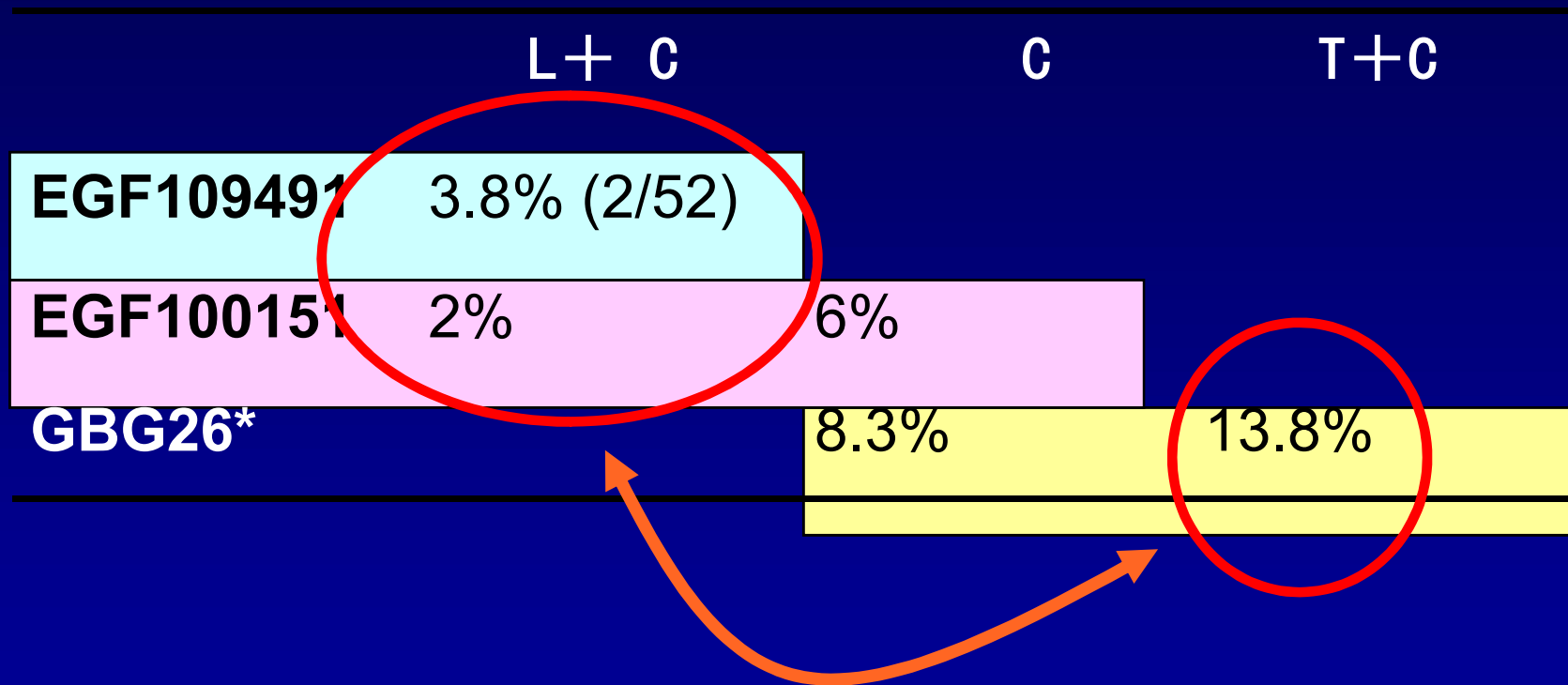
Comparison of results between China (EGF109491) and Global (EGF100151)

L + C (EGF109491) n=52 L + C (EGF100151) n=198

	Investigator	Investigator	IRB
ORR	23 (44.2%)	63 (32%)	47(24%)
CR	0	5 (3%)	1(<1%)
PR	23 (44.2%)	58 (29%)	46(23%)
CBR	30(57.7%)	73 (36.9%)	58 (29.3 %)
(95% CI)	43.2% - 71.3%	30.1% - 44%	23.1% - 36.2%
TTP (m)	6.34	6.2	5.5

数据截止时间: 03,04,2006

Incidence of Brain Metastasis



* Von-Minkwitz, 2008 ESMO #1330

Safety (CTCAE G3-4)

	L + C (EGF109491)	L + C (EGF100151)*
	n=52	n=198
Diarrhea	0%	14%
HFS	0%	12%
Rash	3.8%	2%
Fatigue	1.9%	3%
Nausea	0%	2%
Neutropenia	5.7%	2%
Liver function		
AST/ALT ↑	0%	<1%
Hyperbilirubinaemia	3.8%	<1%

HER2+ MBC: First-line Therapy

- **Trastuzumab**

- Mostly concurrent with chemotherapy
- Start with combination, then stop the chemotherapy

- **Lapatinib**

- With paclitaxel
- With letrozole
- Lapatinib plus capecitabine as Second-line therapy

cNCCN and CSBC Guidelines

Adjuvant Therapy

- Divides BC into biologically important subsets based on HER2 and HR status
- Recognizes differing anatomical and histological risk stratifications
- Identifies a number of chemotherapy regimens appropriate in the adjuvant setting
- Incorporates trastuzumab in HER2 positive BCs
- Recommends adjuvant endocrine therapy in HR-positive disease

cNCCN and CSBC Guidelines MBC Management

- Endocrine therapy in HR-positive and not “rapidly” progressive disease
- Chemotherapy in Visceral or “rapidly” disease
- Trastuzumab + chemotherapy (or lapatinib + chemo-hormones) in HER2 + disease

Thank you for your attention

