

Asian Advanced Gastric Cancer

Hyun Cheol Chung, M.D., Ph.D.
Yonsei Cancer Center
Yonsei University College of Medicine
Seoul, Korea

Disclosure

- Research fund, material: Lilly, MSD, GSK
- Advisor: MSD, Lilly, Celltrion, Taiho, Quintiles
- Speaker: Merck-Serono

I. Incidence

II. Tumor biology and clinical characteristics

III. Host characteristics

IV. Treatment pattern

I-1. Incidence and stage distribution (tumor burden)

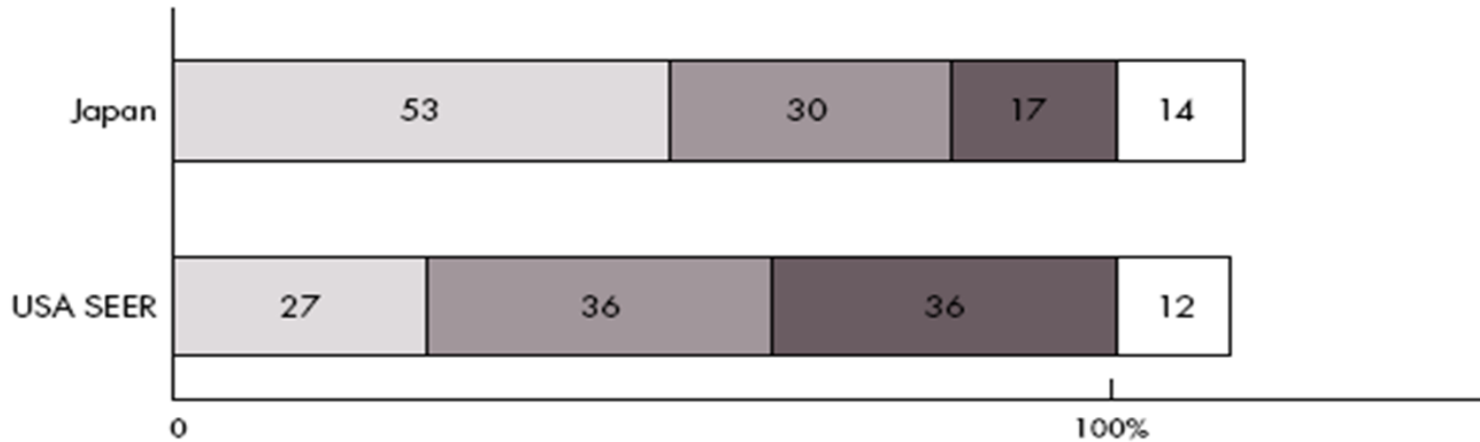


World Health
Organization

World Health
Organization

1995-2000

Localised Regional Distant Unknown



Disease state and survival in Korea (2008-2012)

	Male		Female	
	Frequency	5-yr OS	Frequency	5-yr OS
Localized	57.3%	95.3%	55.8%	93.2%
Regional	24.2%	58.1%	24.3%	58.8%
Distant	11.7%	5.9%	11.7%	5.3%
Unknown	6.9%	48.8%	8.2%	42.6%

100 6000

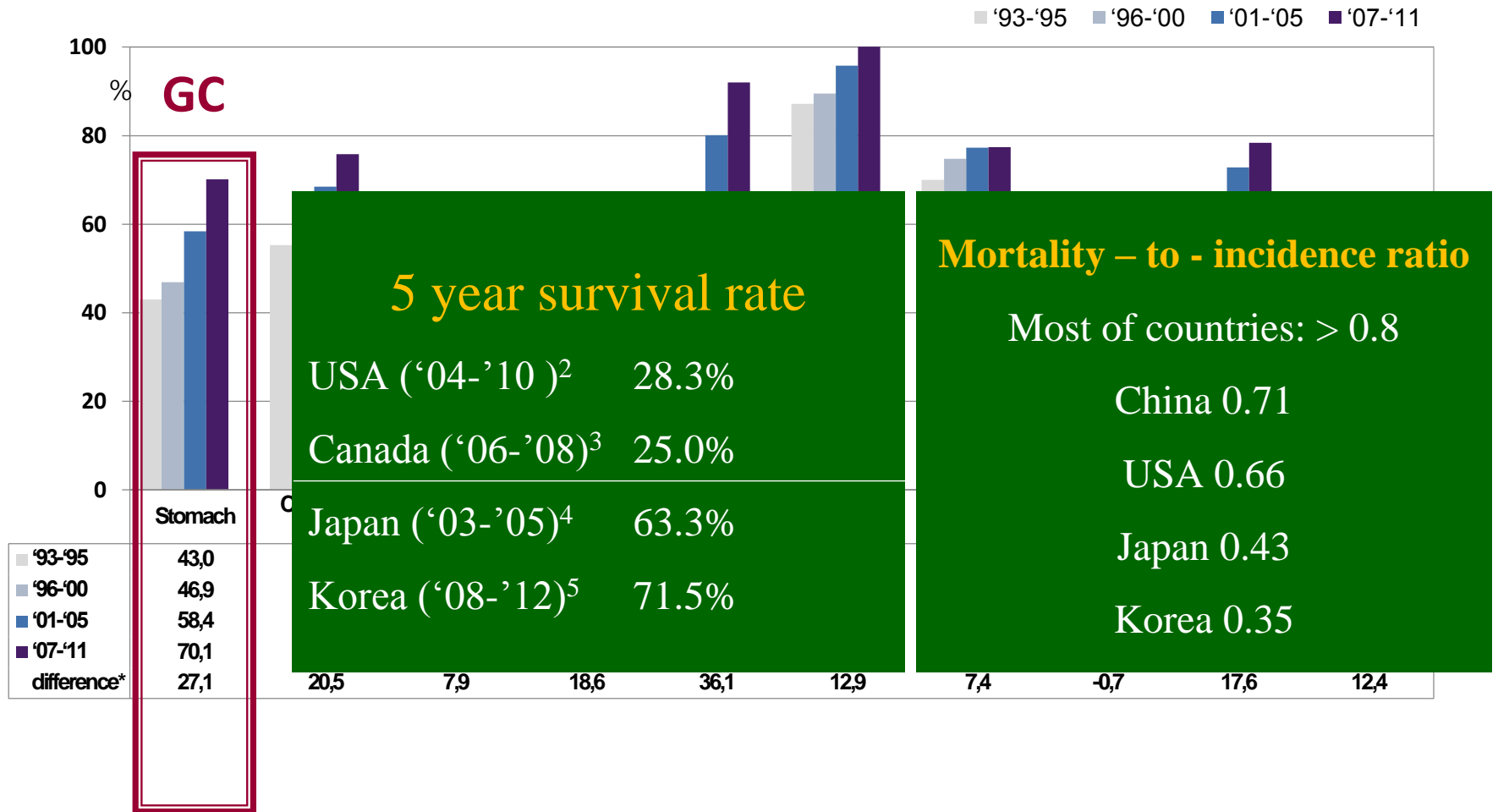
5-year prevalence
Incidence

SINGAPORE
2015

ESMO ASIA

18-21 DECEMBER
SINGAPORE

I-2. Current treatment outcomes



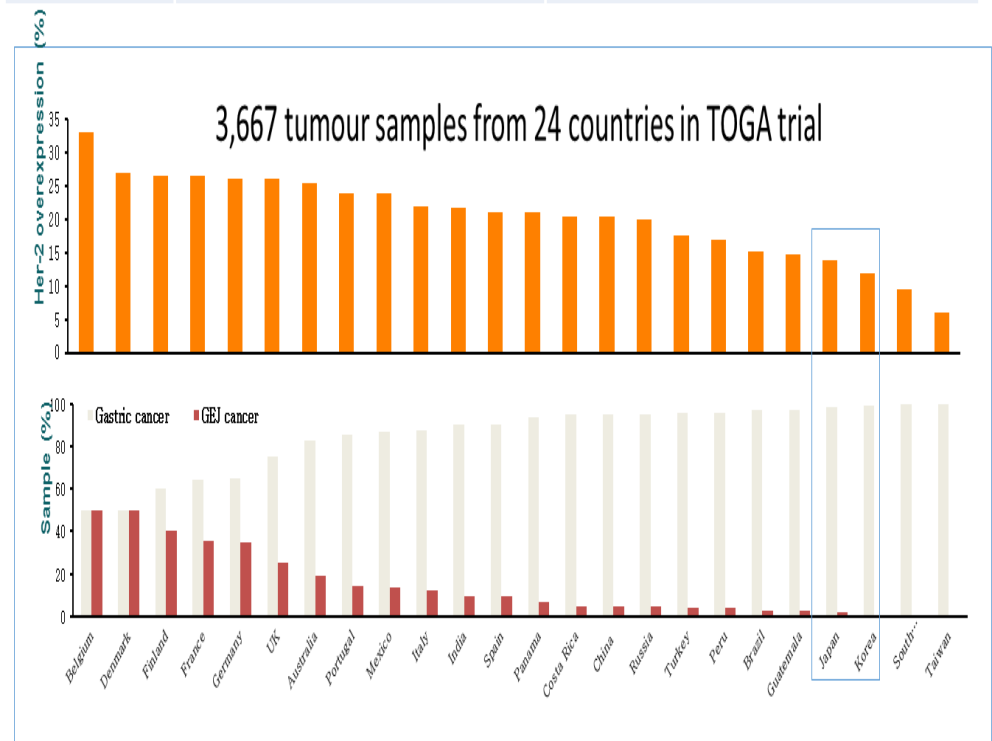
1) Major cancer sites selected based on 2011 crude rates * difference in the cancer survival probability between '93-'95 and '07-'11, 2) Howlader N, Noone AM, et al SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014, 3) Canadian Cancer Society, Statistics Canada and Provincial/Territorial Cancer Registry, Canadian Cancer Statistics 2014, 4) Center for Cancer Control and Information Services, National Cancer Center, Monitoring of Cancer Incidence in Japan - Survival 2003-2005 report 2013, 5) Kyu-Won Jung, Young-Joo Won et al., Cancer Res Treat 2015; 47(2): 123-141

II-1. Histological difference

TABLE 3. Pathological Characteristics

Variable	Country				P
	Korea N = 1646		United States N = 711		
	No. Patients	%	No. Patients	%	
Location of tumor					<0.0001*
GE junction	7	0.40%	131	18%	
Upper	142	9%	146	21%	
Middle	592	36%	189	27%	
Lower	886	54%	232	33%	
Whole	7	0.40%	13	2%	
Unknown	12	1%	—	—	
Differentiation					0.07*
Differentiated	770	47%	361	51%	
Undifferentiated	857	52%	342	48%	
Unknown	19	1%	8	1%	
Lauren classification					<0.0001*
Diffuse	623	38%	203	29%	
Intestinal	729	44%	419	59%	
Mixed	257	16%	79	11%	
N/A or unknown	37	2%	10	1%	

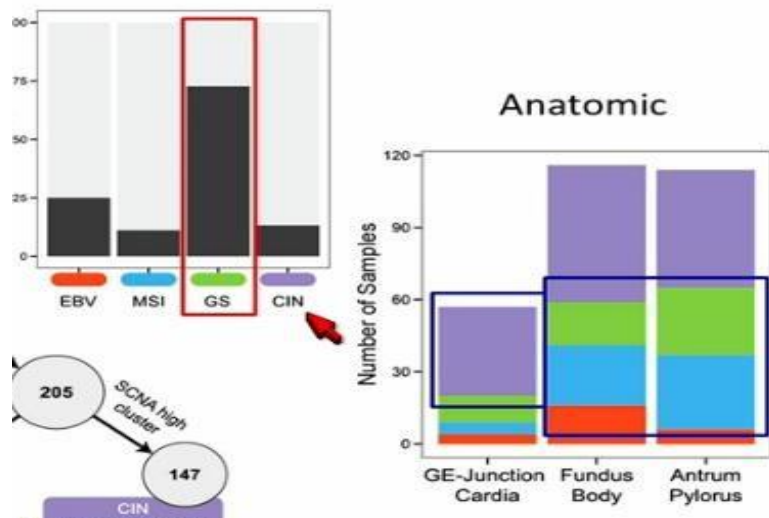
	Korea/Japan	USA
Upper	Undifferentiated, diffuse	More obese, male, intestinal
Lower	Older	Female (1:1)



II-2. Genome and TCGA subtype difference

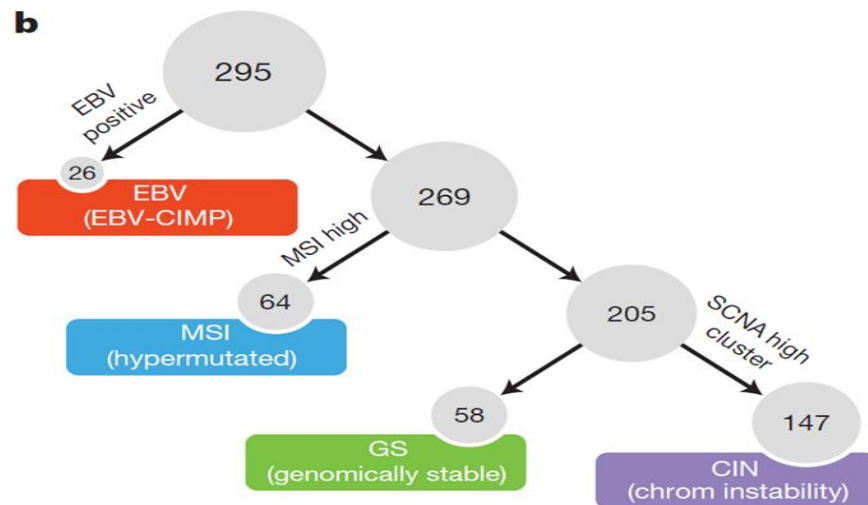
Diffuse type:

Korean 49%
USA 21%



GEJ/Cardia in TCGA

East Asia 9%
USA/Canada 48%



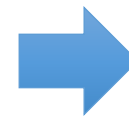
	(%)	EBV-assoc.	MSI-H	GS	CIN
TCGA (total 295)		8.9	21.7	19.7	49.8
YCC* – advanced/metastatic (250)		3.5	4.6	39.4	52.5
YCC* - operable cases, TMA (993)		6.6	11.2	NA	> 25%

➤ Stage-dependent biology and ethnic differences

III. Host characteristics

TABLE 1. Patient Demographics 1995–2005

	Country		<i>P</i>
	Korea	United States	
No. patients	1646	711	
Male	1096	425	0.002*
Female	550	286	0.002*
Median age (yr) (range)	59 (18–91)	69 (22–96)	<0.0001 [†]
BMI (kg/m ²) [‡] median (range)	22.6 (13.7–35.9)	25.4 (14.1–47.6)	<0.0001 [†]
Race			
Caucasian	—	538 (76%)	
Black	—	45 (6%)	
Asian	1646 (100%)	74 (10%)	
Hispanic	—	53 (7%)	
Other	—	1 (0.1%)	
Family history			<0.0001*
Yes	87 (5%)	92 (13%)	
No	1559 (95%)	579 (81%)	
Unknown	—	40 (6%)	

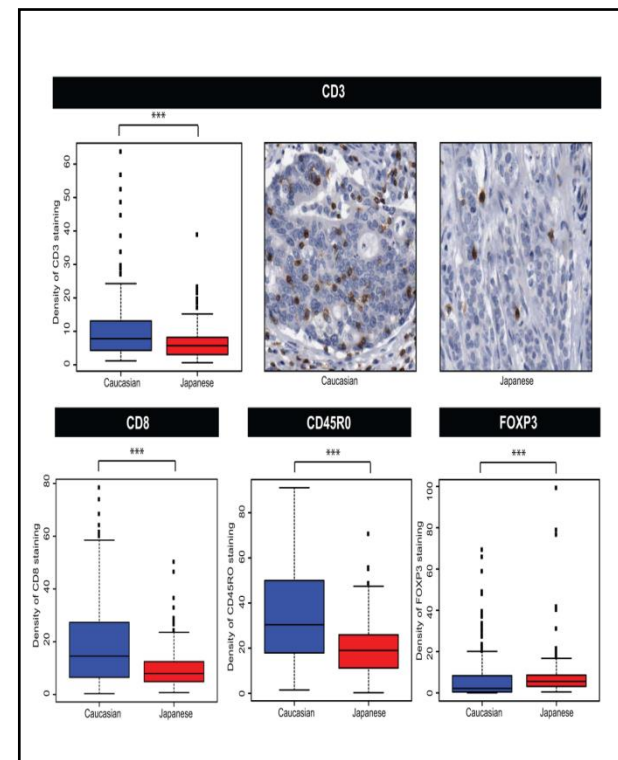
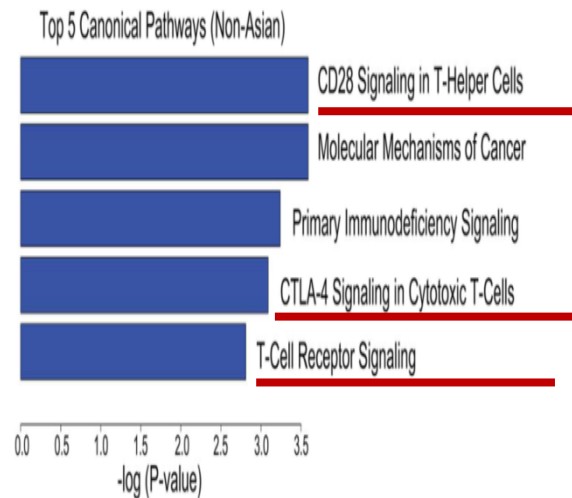
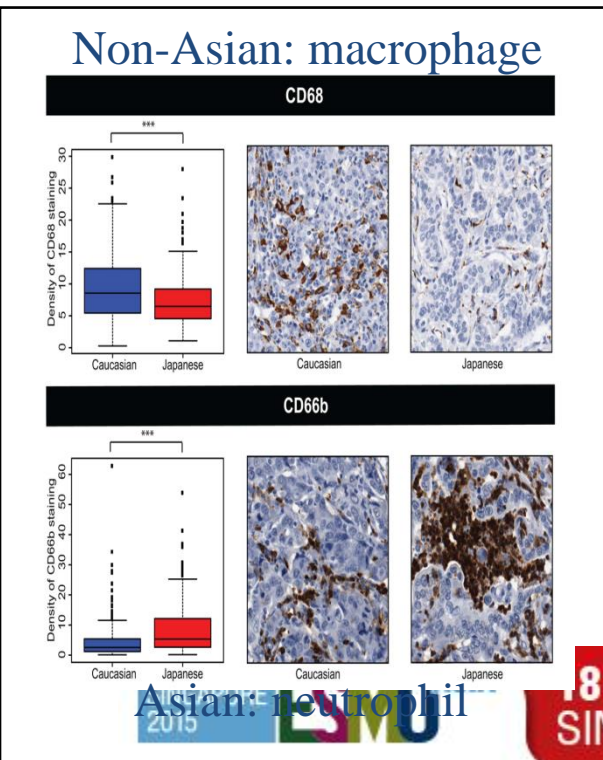
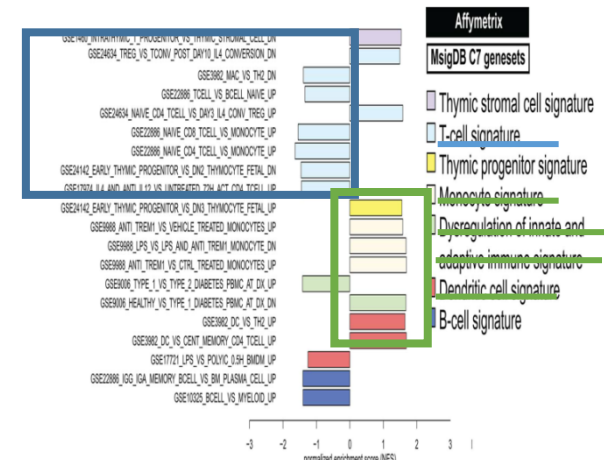
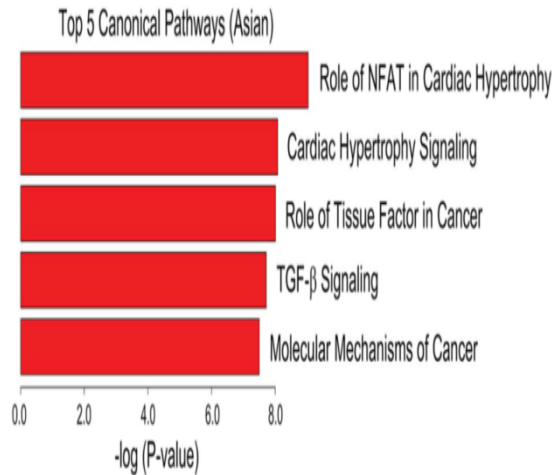
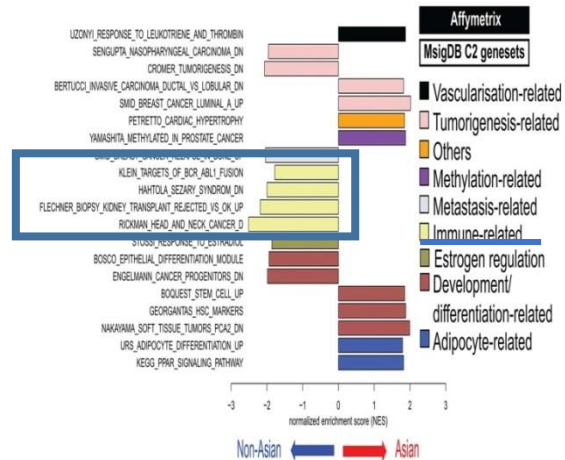


Affects chemotherapy outcome!



Genetic family history vs Environmental family history

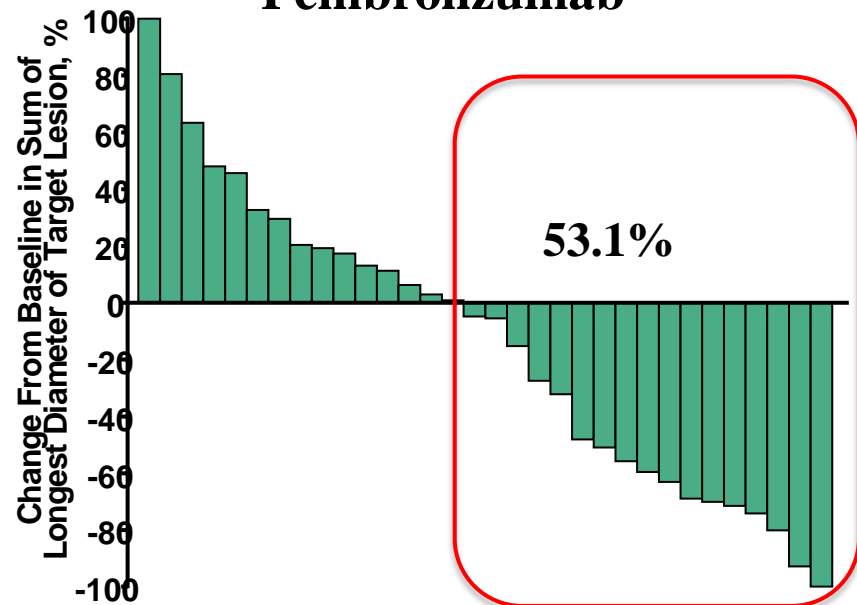
III-1. Immune & micro-environmental factors



18-21 DECEMBER
SINGAPORE

III-2. Immune checkpoint inhibitors

Pembrolizumab

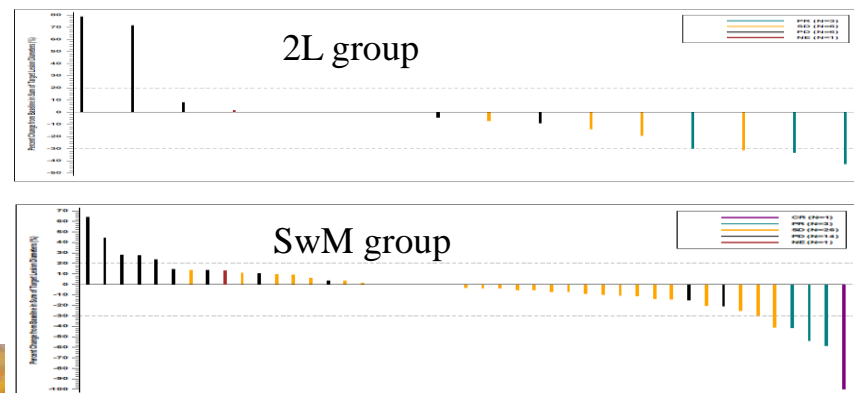


	Total N = 39	Non-Asian n = 20	Asian n = 19
ORR, ^a % (95% CI)	30.8 (17.0-47.6)	30.0 (11.9-54.3)	31.6 (12.6-56.6)
Best overall response, n (%)			
Complete response	0	0	0
Partial response	12 (30.8)	6 (30.0)	6 (31.6)
Stable disease	5 (12.8)	1 (5.0)	4 (21.1)
Progressive disease	21 (53.8)	12 (60.0)	9 (47.4)
Not evaluable	1 (2.6)	1 (5.0)	0

Durvalumab



Avelumab



IV. Treatment pattern

- **Screening program** (early diagnosis, low tumor burden, long-term survival): EGC 68% at 2004 (Japan), 46-67% (Korea)
- **Palliative chemotherapy**: Doublet vs triplet, various regimens, lines of treatment
- **Supportive care**: GI-GU-Biliary stent, draining pigtail, palliative radiotherapy, hyperalimentation, pain control, anti-emetics

IV-1. Trends in palliative chemotherapy

Asia

**(5-FU analogue + platinum)
(FP/XP/SP/FOLFOX/CapOX/SOX)**

Adding trastuzumab in Her-2 + patients

North America

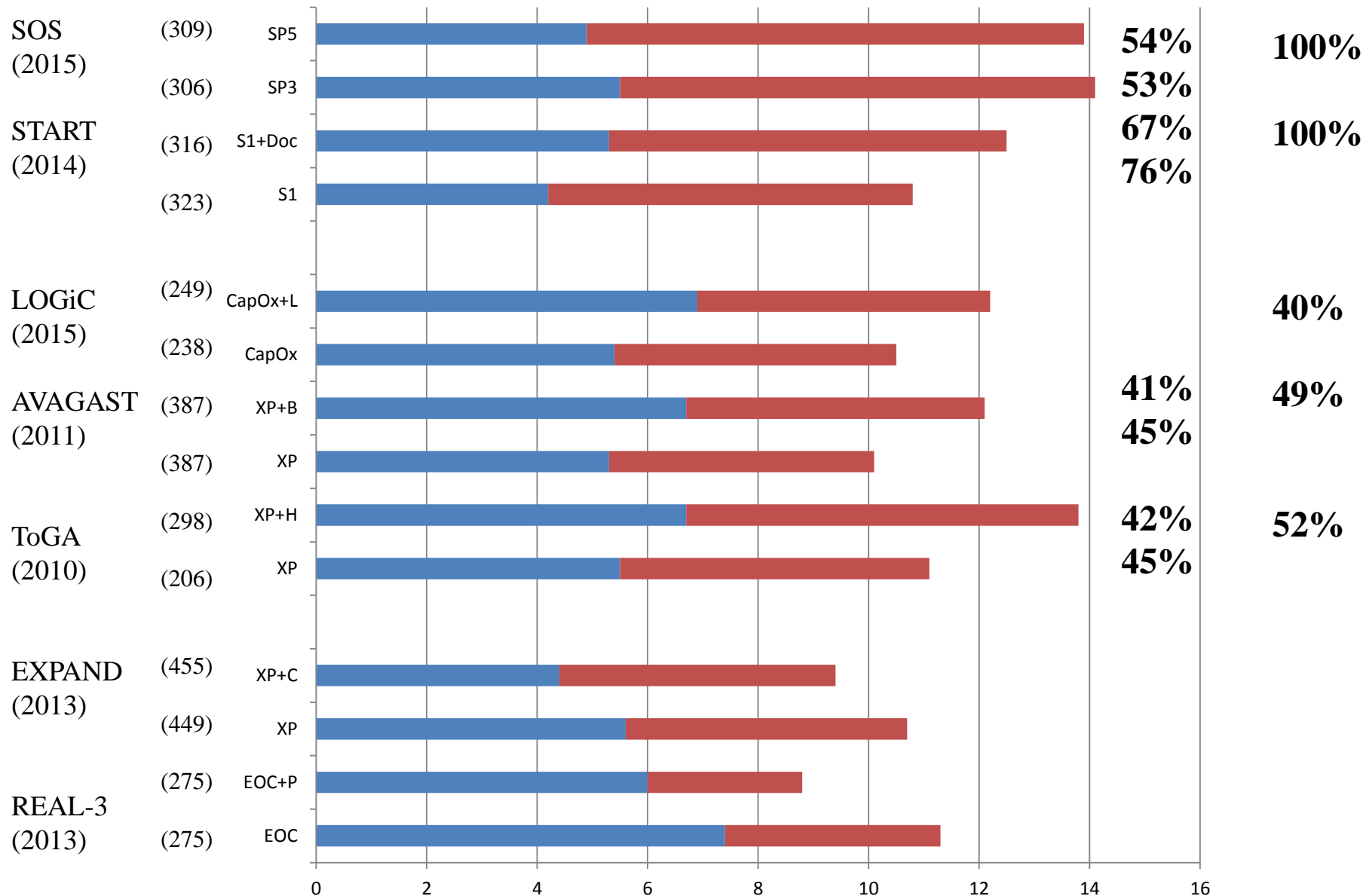
(5-FU/cisplatin, DCF)

Europe

(ECF/EOX)

2nd line

Asian



IV-2. Regional difference in OS

FLAGS

ToGA

AVAGAST

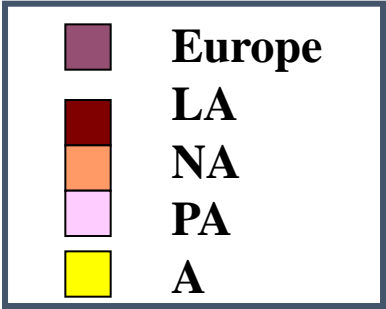
STASRT

LOGIC

RAINBOW

America > Europe > Asia

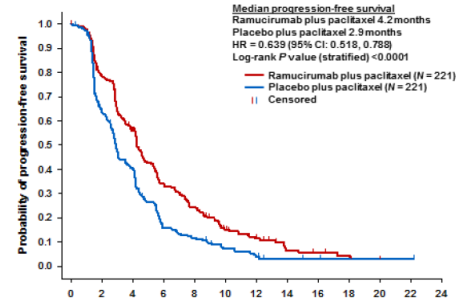
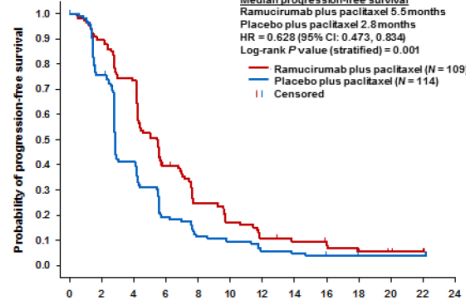
• A : 12.1 → 13.9
• E : 8.6 → 11.1
• AM: 6.8 → 11.5



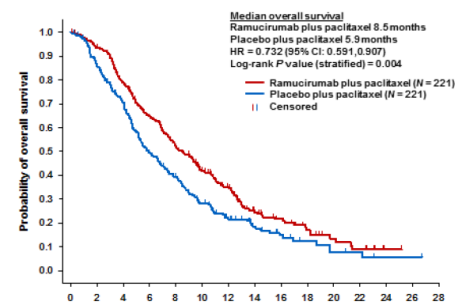
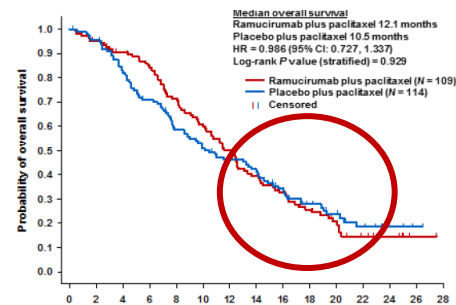
East Asian

Non-East Asian

PFS



OS



Without subsequent treatment

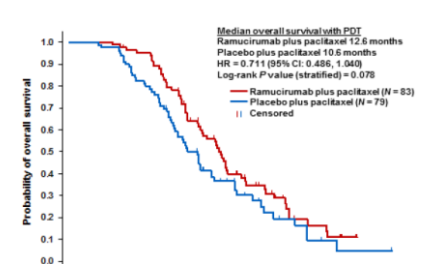
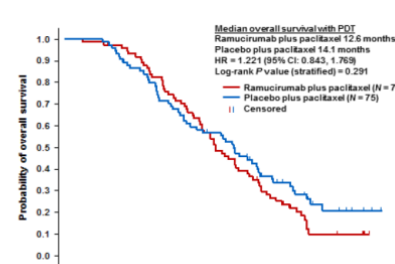
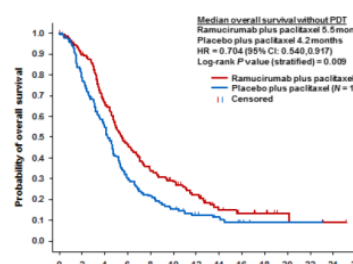
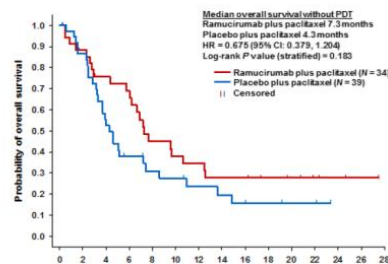
With subsequent treatment

East Asian

Non-East Asian

East Asian

Non-East Asian



IV-3. Culture and policy-related issues

- Herbal medicine
- Drug availability and reimbursement
- Cultural uniqueness:
 - continued chemotherapy with good PS: 4th, 5th line,
 - clinical trials
- Different attitude for hospice care (short survival after PD)





Americans had access to
33% More new cancer
therapies than Europeans



Europeans wait up to
3 Years Longer for new
therapies than Americans

Rate of new treatment use accounts for **Up to 19%**
of the difference in 5-year cancer survival

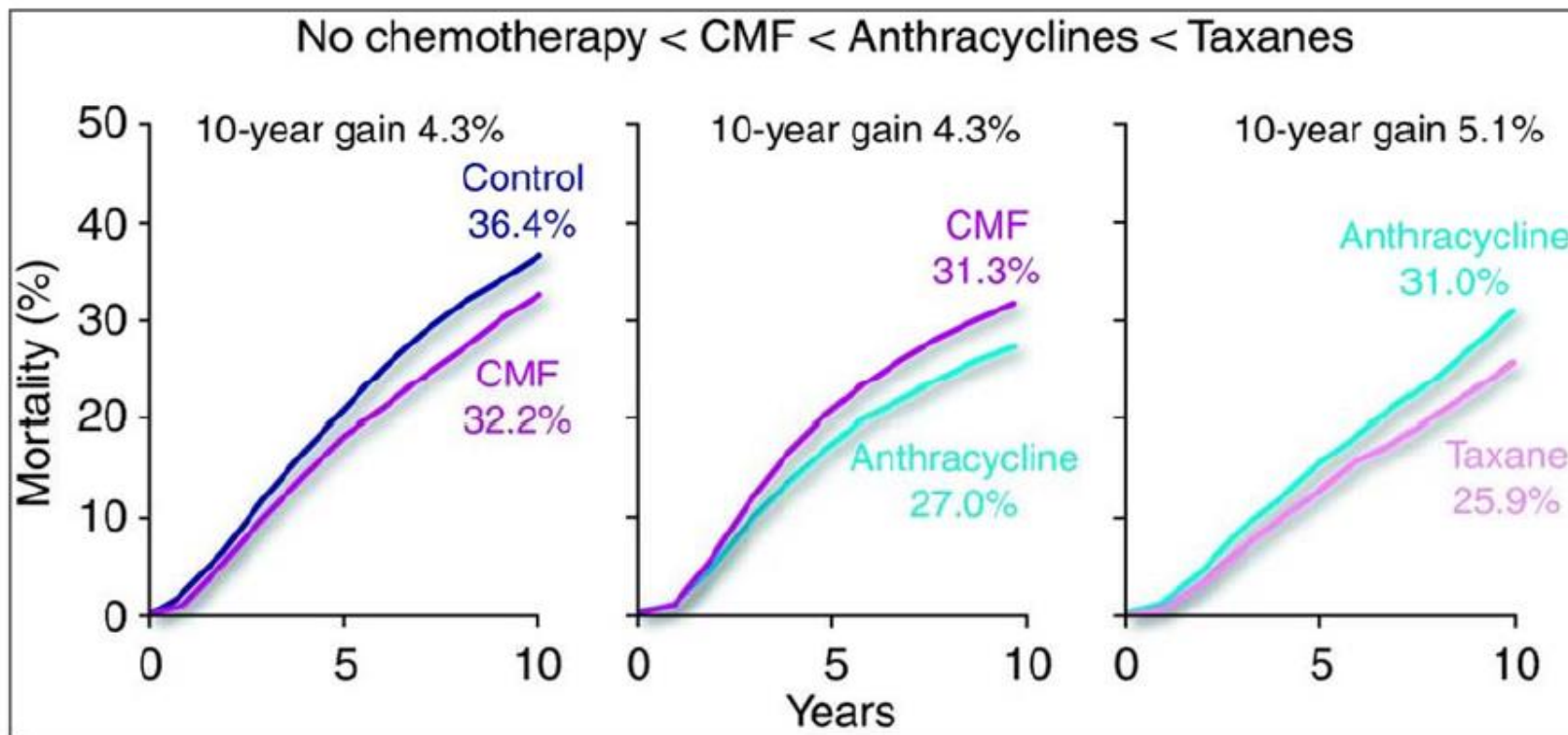


Figure 1. Stepwise improvements in efficacy of chemotherapy for early-stage breast cancer.⁶

PFS

ToGA

Rainbow

Apatinib

Keynote-012

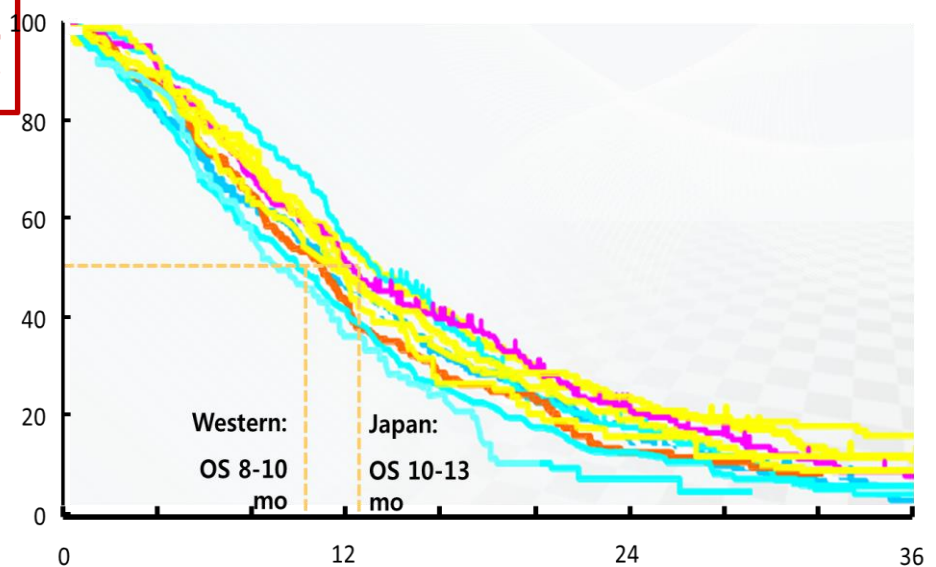
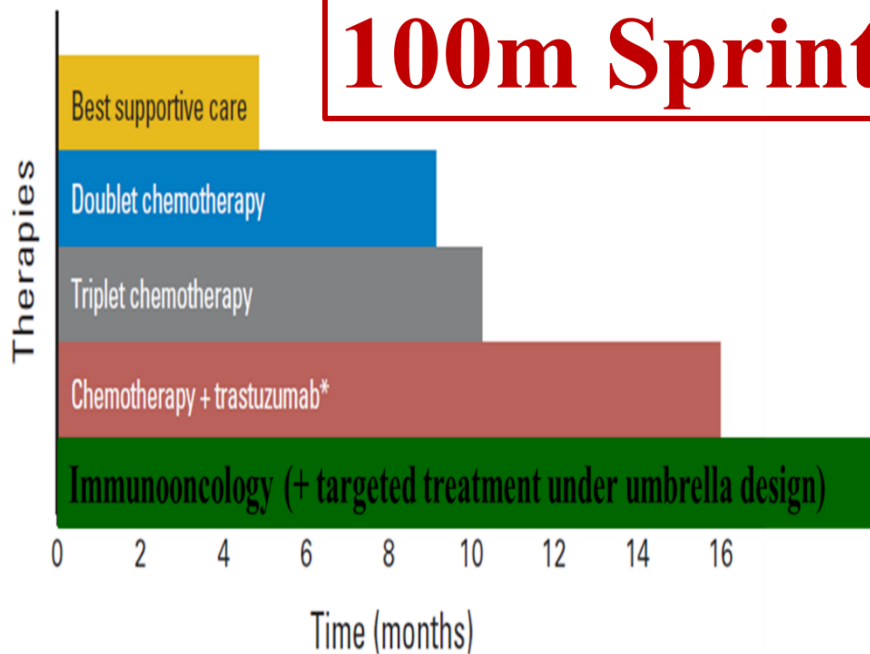
1st line : 6.7 Mo

2nd line : 4.4 Mo

3rd line : 3.7 Mo

4th line : 1.9 Mo

100m Sprint



1. Ohtsu A, J Gastroenterol 2008

Longer PFS/Better PS → Next regimen (Relay Race)

SINGAPORE
2015

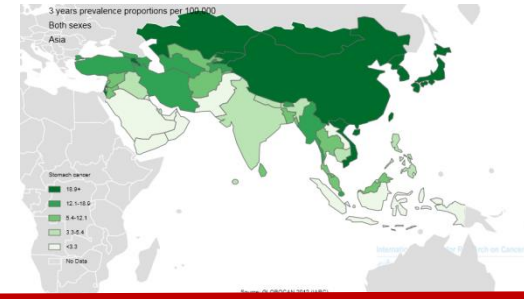
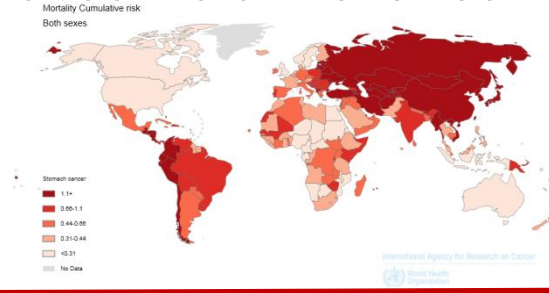
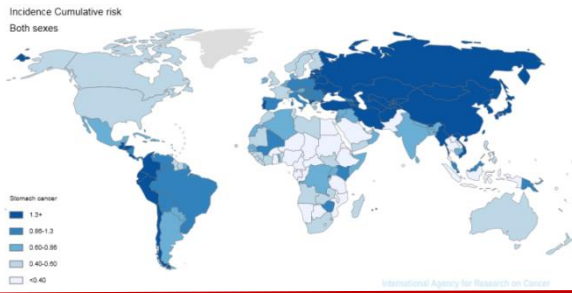
ESMO
ASIA

18-21 DECEMBER
SINGAPORE

Summary

	EAST	WEST
Incidence/prevalence/Age	High/50s	Low/60s
Tumor burden/stage	Low	High
Location	distal	proximal
Histology	diffuse	intestinal
TCGA		
EBV	4-7%	9%
MSI	5-11%	22%
GS	39%	20%
CIN	53%	50%
Immune	Treg	T cell pathway
	EAST	WEST
Localized (National screen)	Better endoscopist, radiologist	
Regional (D2)	Better surgeon	
Systemic		Better drug reimburse
Survival	Better in stage II-IV	Similar in stage I

Outcome difference



1st line : 6.7 Mo

2nd line : 4.4 Mo

3rd line : 3.7 Mo

4th line : 1.9 Mo

- Tumor burden

- Tumor genomics
& biology

- Culture & hope

- Drug
availability

Asian cancer : $\geq 3^{\text{rd}}$ line treatment (12~15 months)

Non-Asian cancer : $\leq 2^{\text{nd}}$ line treatment (8~10 months)



Gastric Cancer Center

Acknowledgement

Medical Oncology: Hyun Cheol Chung, Hyo Song Kim, Min Kyu Jung, Seung Hoon Beum
Surgical Oncology: Sung Hoon Noh, Woo Jin Hyung, Jae Ho Jeong, Hyung Il Kim
Gastroenterology: Yong Chan Lee, Sang Gil Lee, Hyun Soo Jung
Pathology Hyun Ki Kim, Radiology: Jun Seok Lim

“Gastric cancer is heterogeneous, but
a globally manageable disease.”



ESMO-CSCO-JSMO-KACO Joint Symposium



Happy Holidays & Happy New Year



SINGAPORE
2015

ESMO ASIA

18-21 DECEMBER
SINGAPORE