

# Neoadjuvant Chemotherapy

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**CNUH**

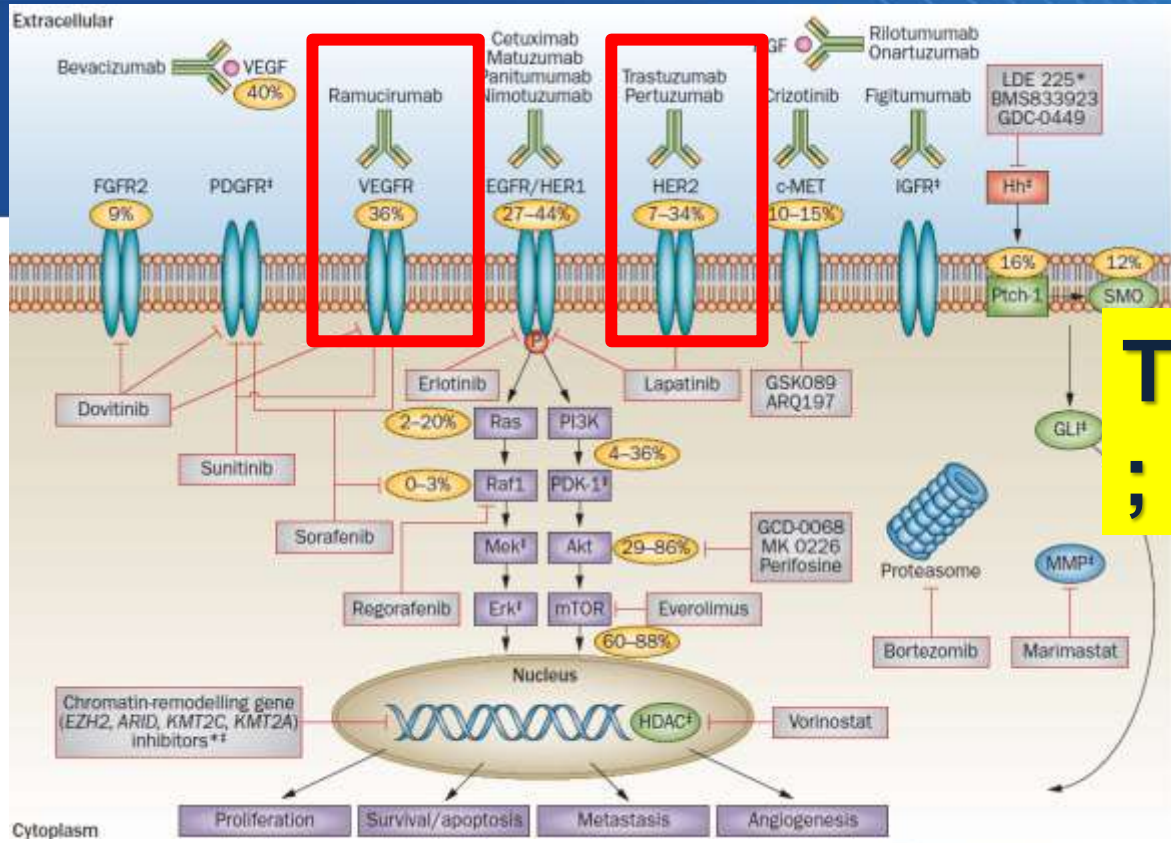


# CONTENT

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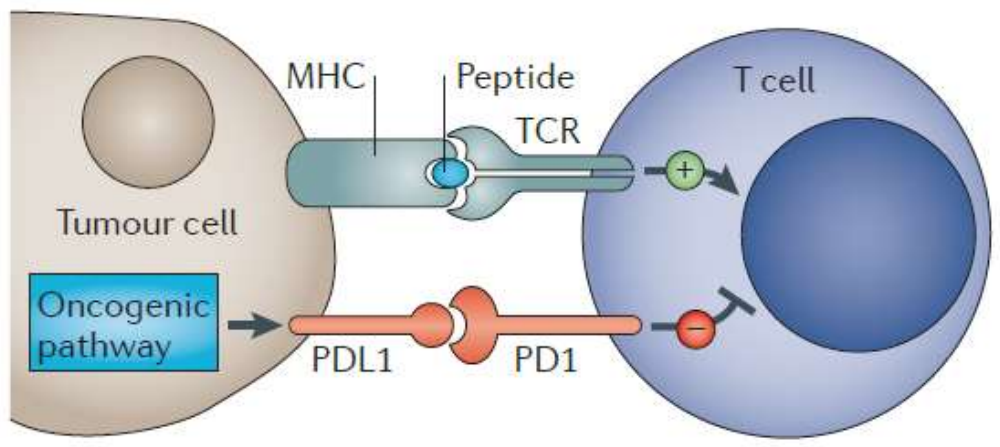


1. 서론
2. 동서양의 위암의 차이
3. 선행치료의 장단점
4. 선행항암치료에 대한 임상 연구
5. 반응평가 및 예후에 미치는 인자
6. 결론



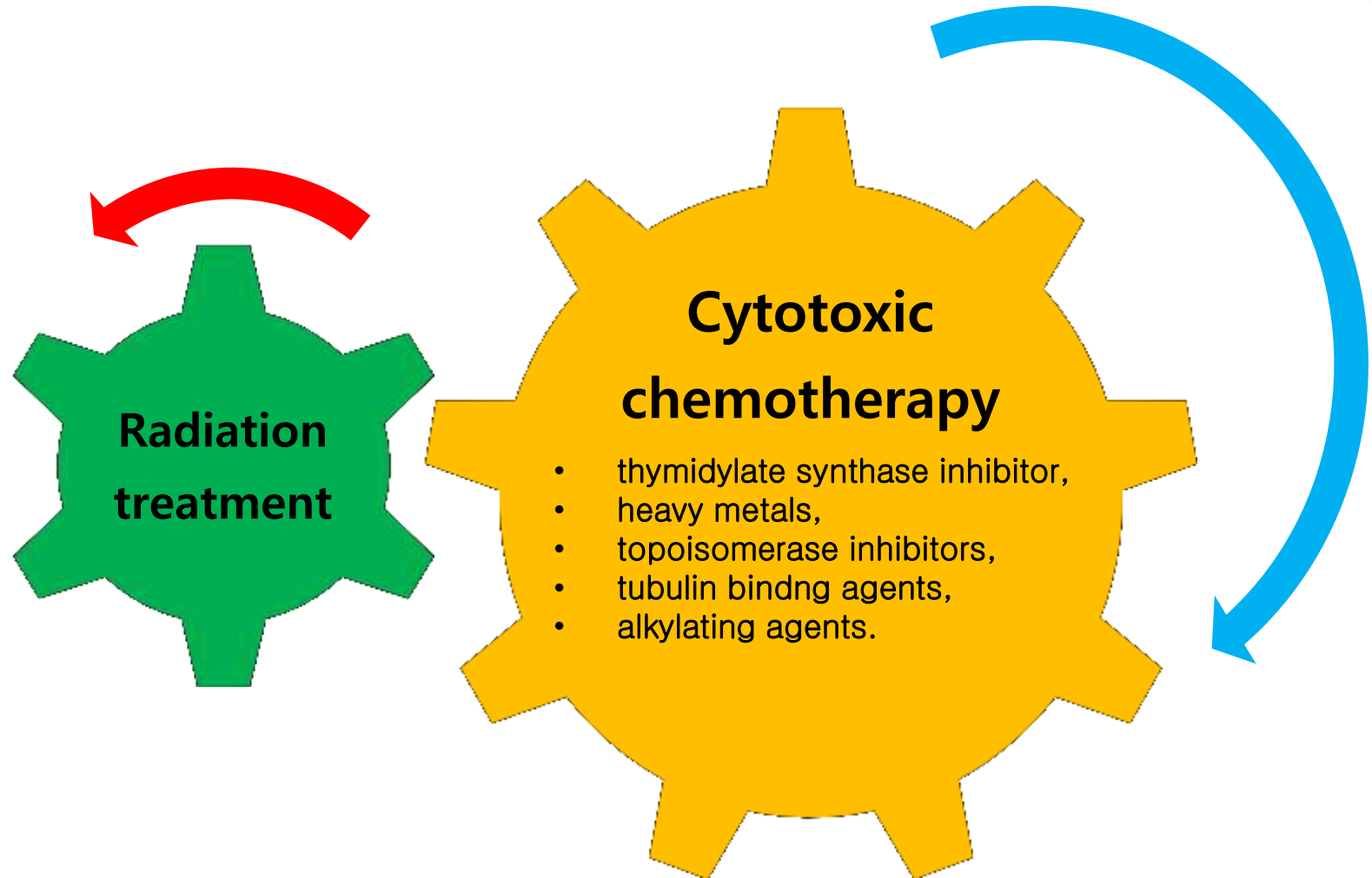
**Targeted therapy ; palliative setting**

**PD-1/PD-L1 pathway inhibitor ; Ongoing**



Nature Reviews Clin Oncol 2013;10:643-55  
 Pardoll D.M. Nat Rev Cancer 2012;12:252-64

# Neoadjuvant therapy



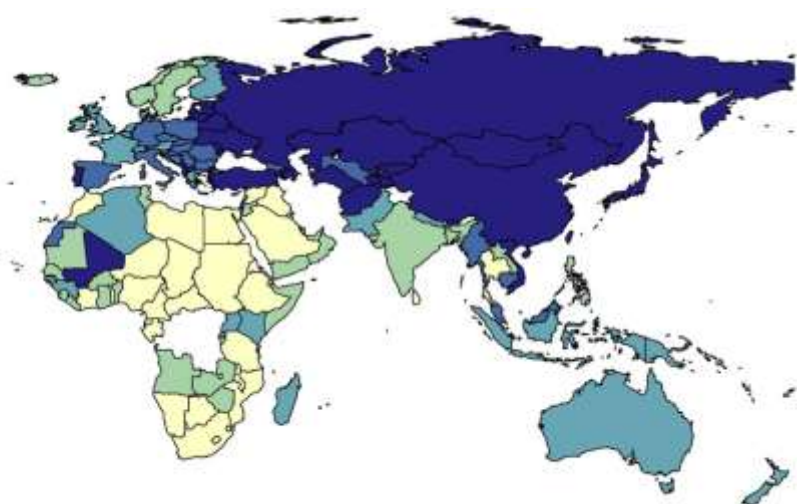
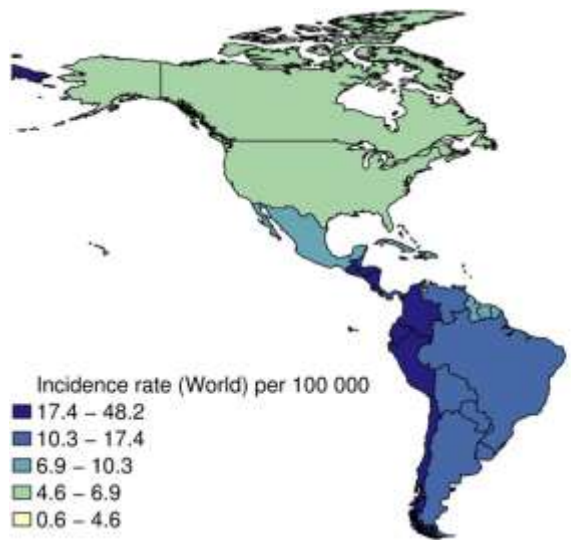
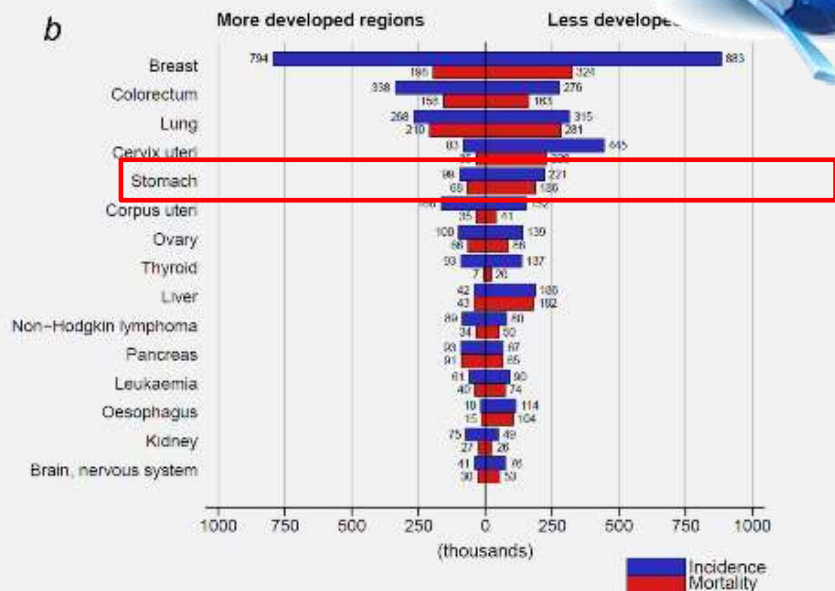
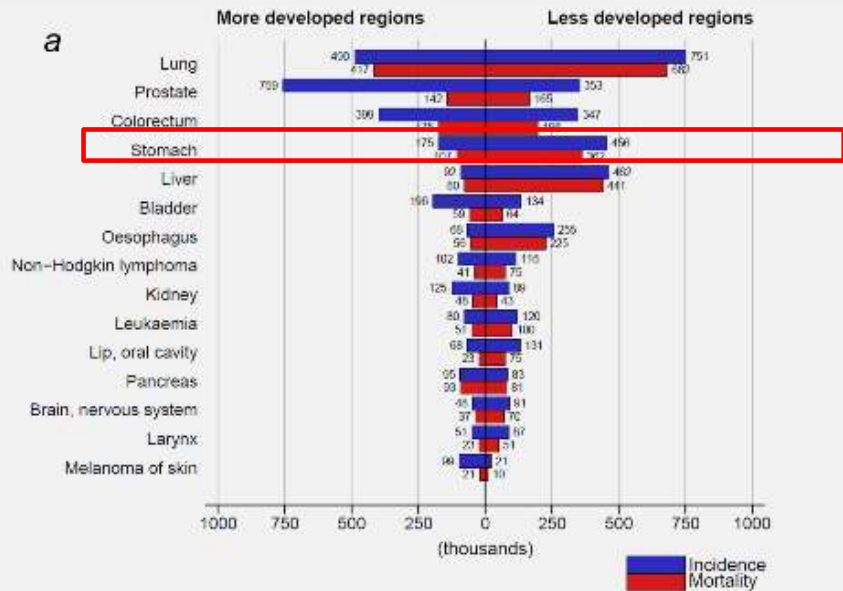
# Limitation in the study of neoadjuvant treatment



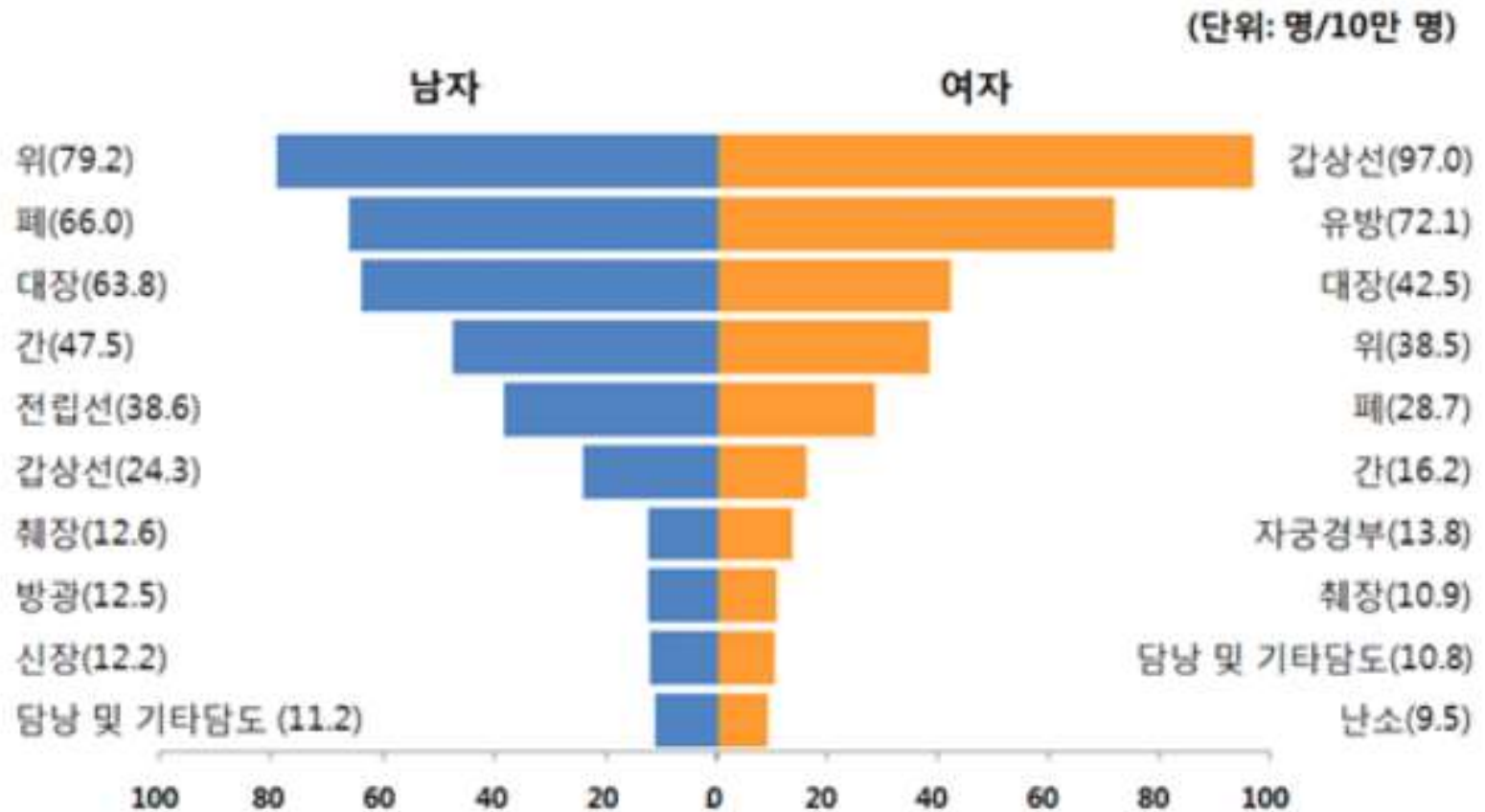
- **Small sample size**
- **EGJ cancer with esophageal extension**
  - : Esophageal cancer( 7<sup>th</sup> edition of the AJCC)
- **Heterogeneity of chemotherapy regimens & dose**
- **Diversity of preoperative staging modalities**
- **Not covered in health insurance**



# Gastric cancer is the third leading-cause of cancer related mortality worldwide



# Cancer incidence rate in the korea: 2014



# Therapeutic strategy for stage II/III gastric cancer



- Surgery is the mainstay of treatment for locally advanced gastric cancer.
- **R0 resection** is the only way leading to long-term survival.
- Despite radical surgery, a proportion of patients undergoing curative resection relapse with local and systemic recurrence, which leads to poor survival.
- For better outcome, combinations of **optimal perioperative approach** with curative surgery have been tried

Tumor Depth	JCGC Stage	No. of Tumors	No. of Recurrences	Lymph Node Metastasis and Regional Failure		Hematologic	
				Peritoneum		No. of Tumors	%
T1	M	1,063	2	0	0	2	0.2
	SM	881	18	6	3	9	1.0
T2	MP	436	45	10	9	26	5.9
	SS	325	74	15	28	31	9.5
T3	SE	1,232	625	146	330	149	12.1
T4	SI	724	562	173	283	106	14.6
Overall, no.		4,683	1,326	330	635		323
Overall, %			28.3	7.0	13.6		6.9



# Perioperative therapeutic strategies



- Type of surgical procedure ( = extent of resection/LN dissection ,

- Adjuvant chemoradiotherapy

*Macdonald JS, et al. N Engl J Med 2001; 345: 725*

- Adjuvant chemotherapy

*Sakuramoto S, et al. N Engl J Med 2007; 357: 1810*

*Bang YJ, et al. Lancet 2012; 379: 315*

- **Neoadjuvant/perioperative chemotherapy**

*Cunningham D, et al. N Engl J Med 2006; 355: 11*

*Ychou M, et al. J Clin Oncol 2011; 29: 1715*

- Neoadjuvant chemoradiotherapy

*Stahl M, et al. J Clin Oncol 2009; 27: 851*

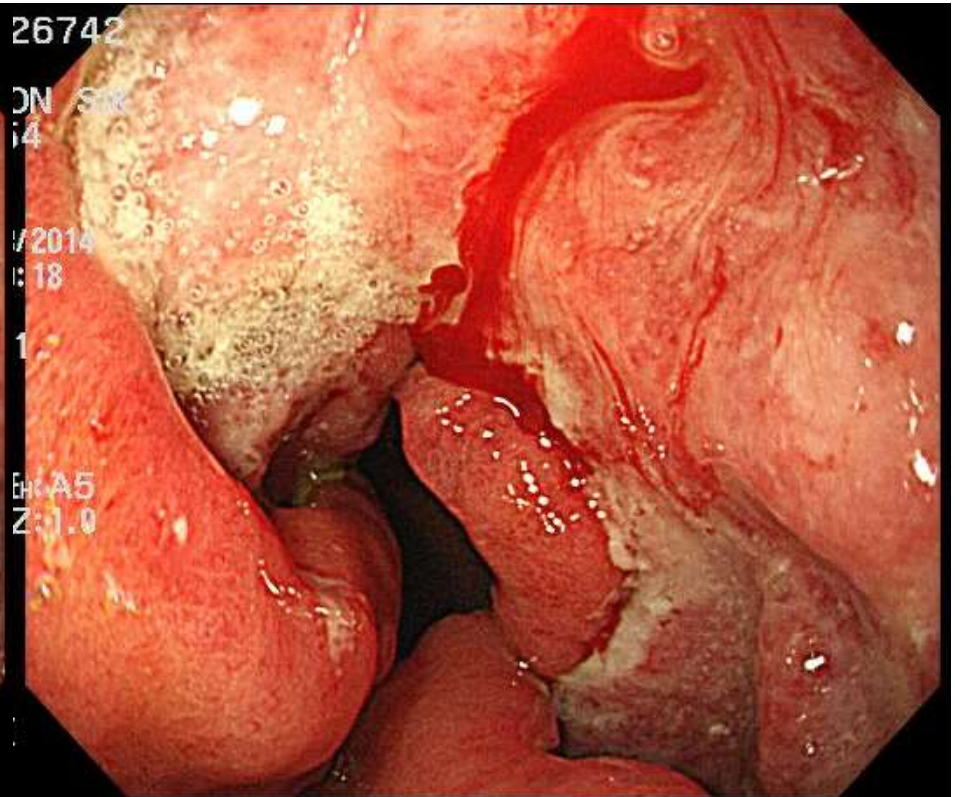
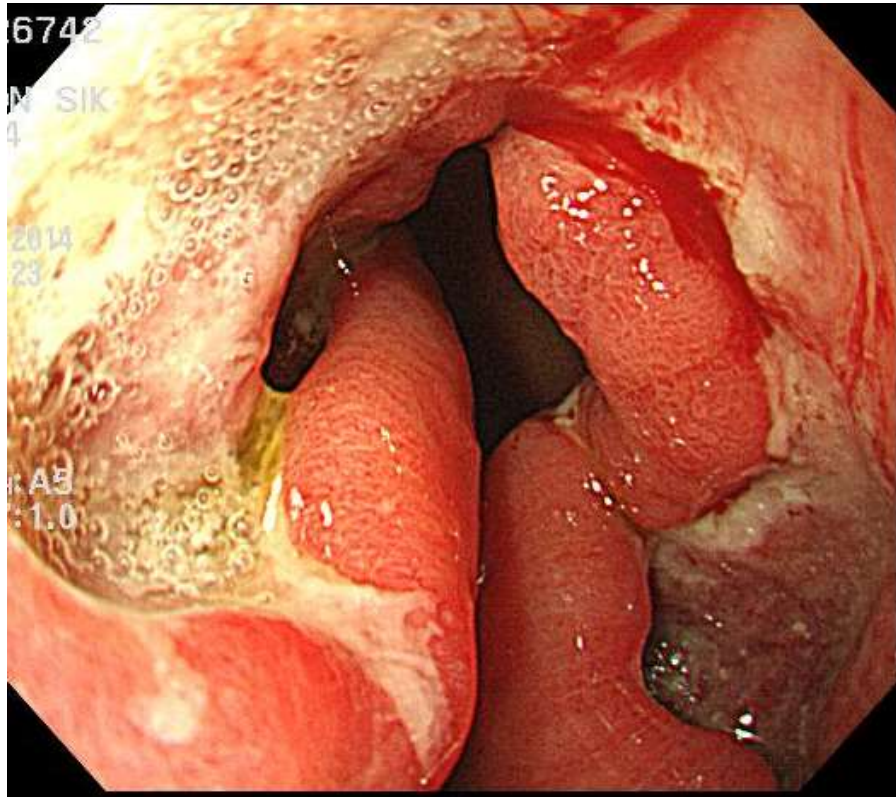
# Locally-advanced, marginally resectable gastric cancer



- Defined by tumor size (T) and lymph node involvement (N). T3 and N positive tumors are considered locally-advanced.
- Advanced large type 3 ( $\geq 8$  cm) or 4 (linitis plastica) tumors para-aortic lymph node metastases ( $\geq 1$  cm) and/or bulky nodal metastases ( $\geq 3$  cm or  $\geq 1.5$  cm  $\times$   $\geq 2$  nodes) surrounding the celiac artery and its branches are considered marginally resectable

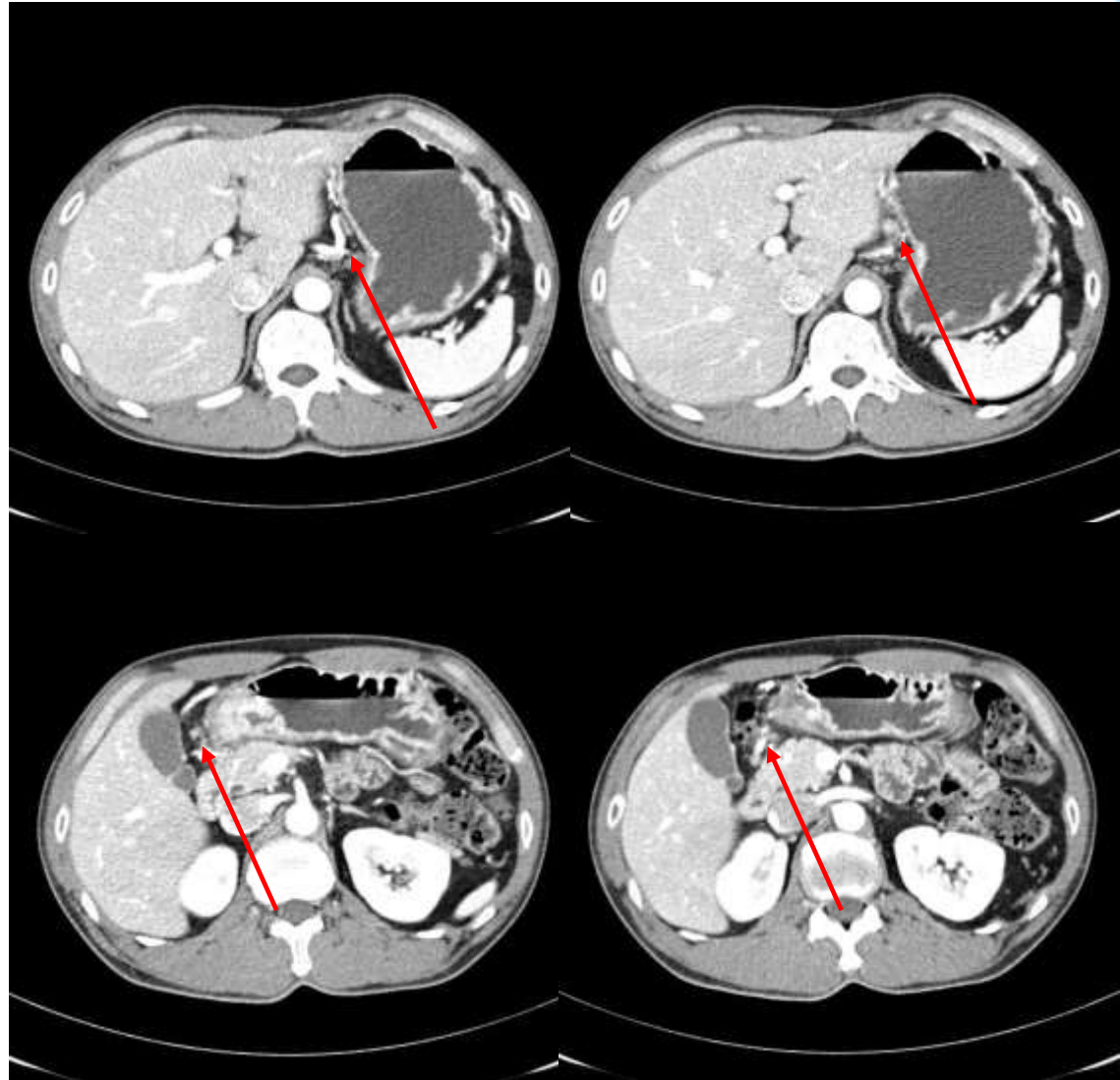
	N0	N1	N2	N3
T1a (M), T1b (SM)	IA	IB	IIA	IIB
T2 (MP)	IB	IIA	IIB	IIIA
T3 (SS)	IIA	IIB	IIIA	IIIB
T4a (SE)	IIB	IIIA	IIIB	IIIC
T4b (SI)	IIIB	IIIB	IIIC	IIIC
M1 (Any T, Any N)	IV			

# 54/M

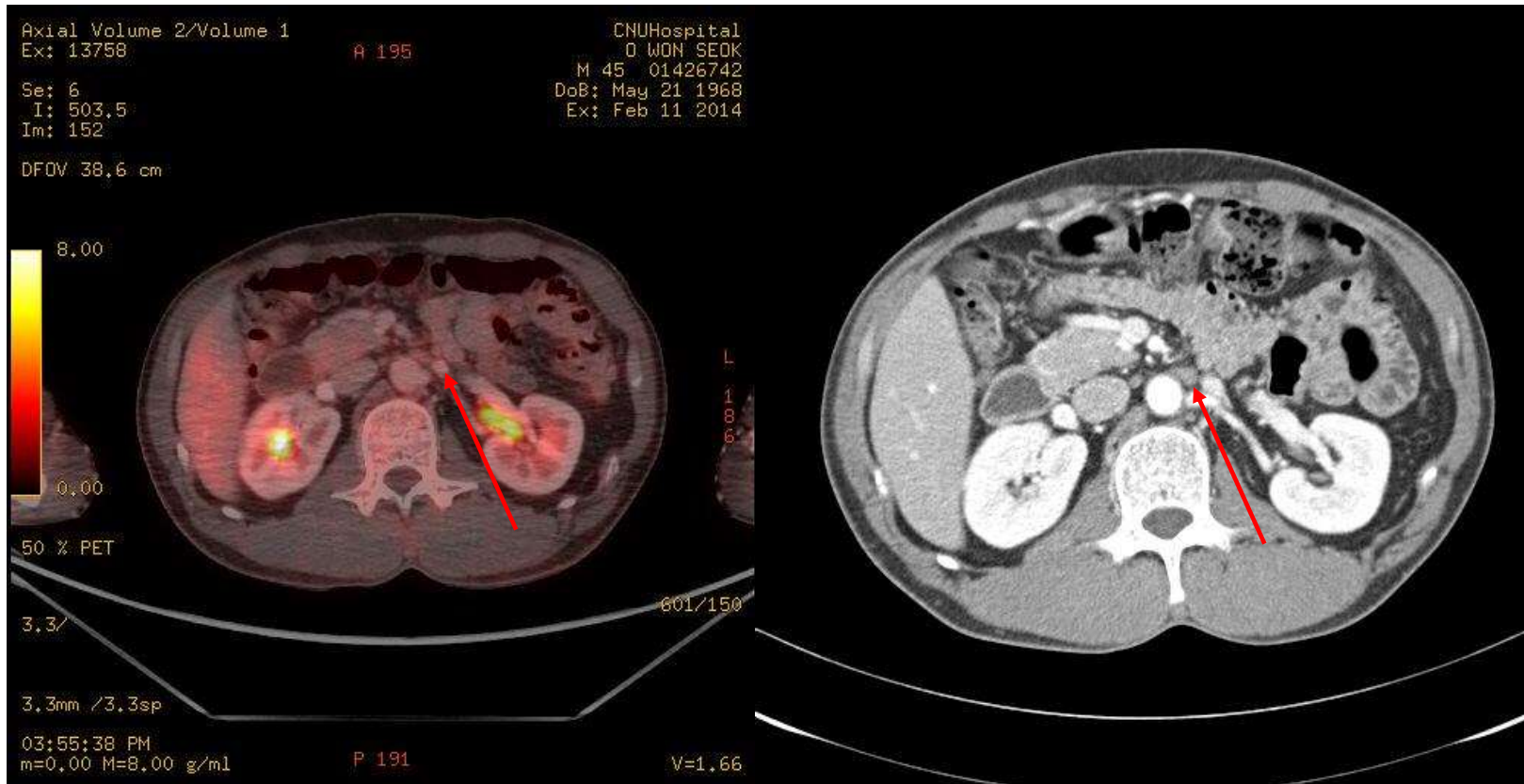




# Before Neoadjuvant Treatment



# Initial cStaging [T4aN2M1, IV]





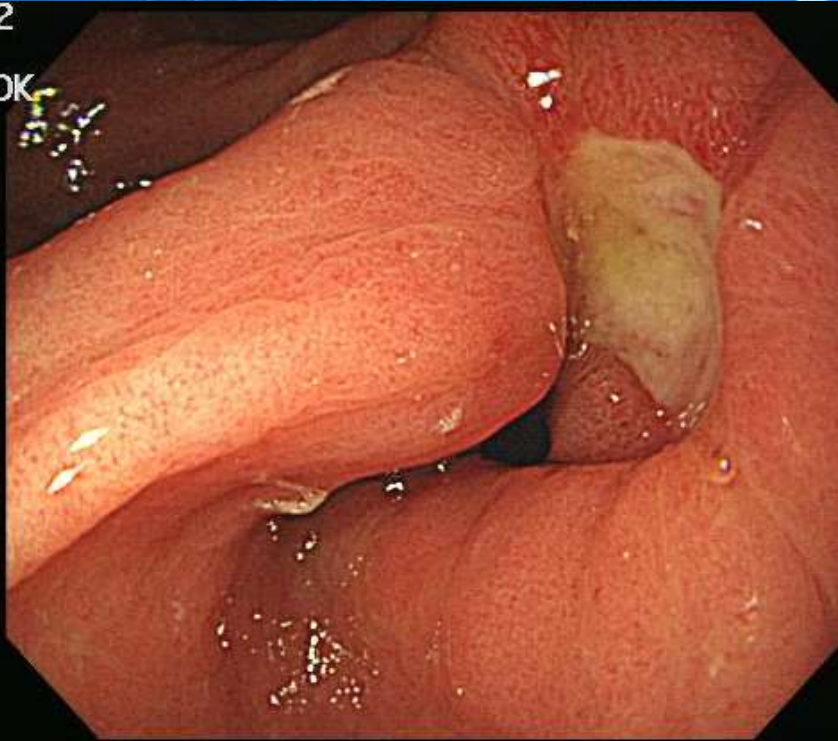
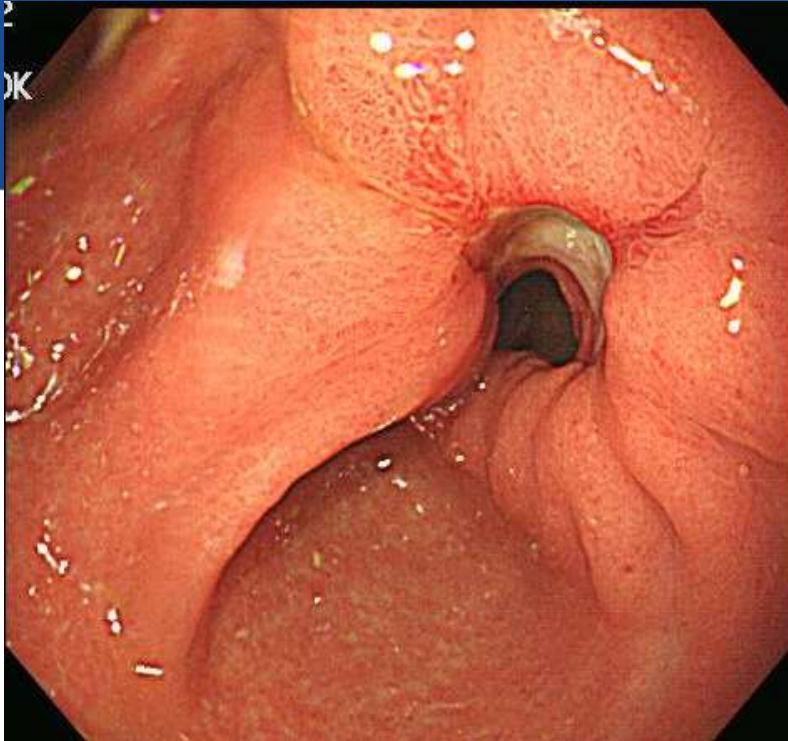
# NAC regimen & schedule



Regimen	Dose	Duration
Docetaxel	50mg/m <sup>2</sup>	D1
Oxaliplatin	100mg/m <sup>2</sup>	D1
S-1	40mg/m <sup>2</sup>	D1-14

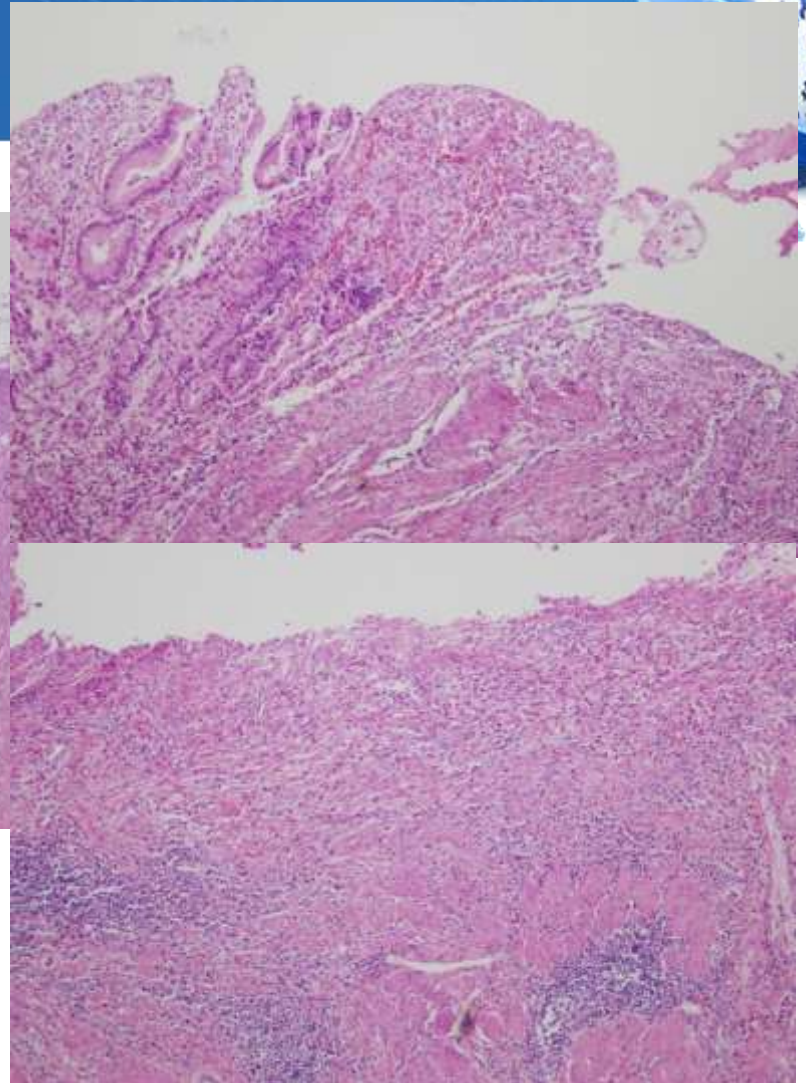
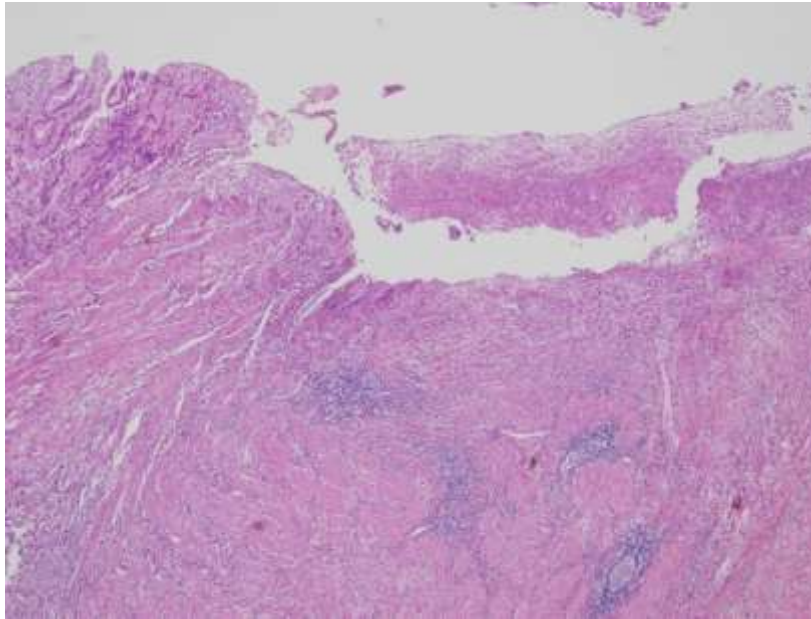
Every 3 weeks for three cycles.

- 2014.02.13 ~ 02.26) #1 DOS
- 2014.03.07 ~ 03.20) #2. DOS
- 2010.03.28 ~ 04.10) #3. DOS



**Totally laparoscopic RSG with Roux-en-Y GJ**



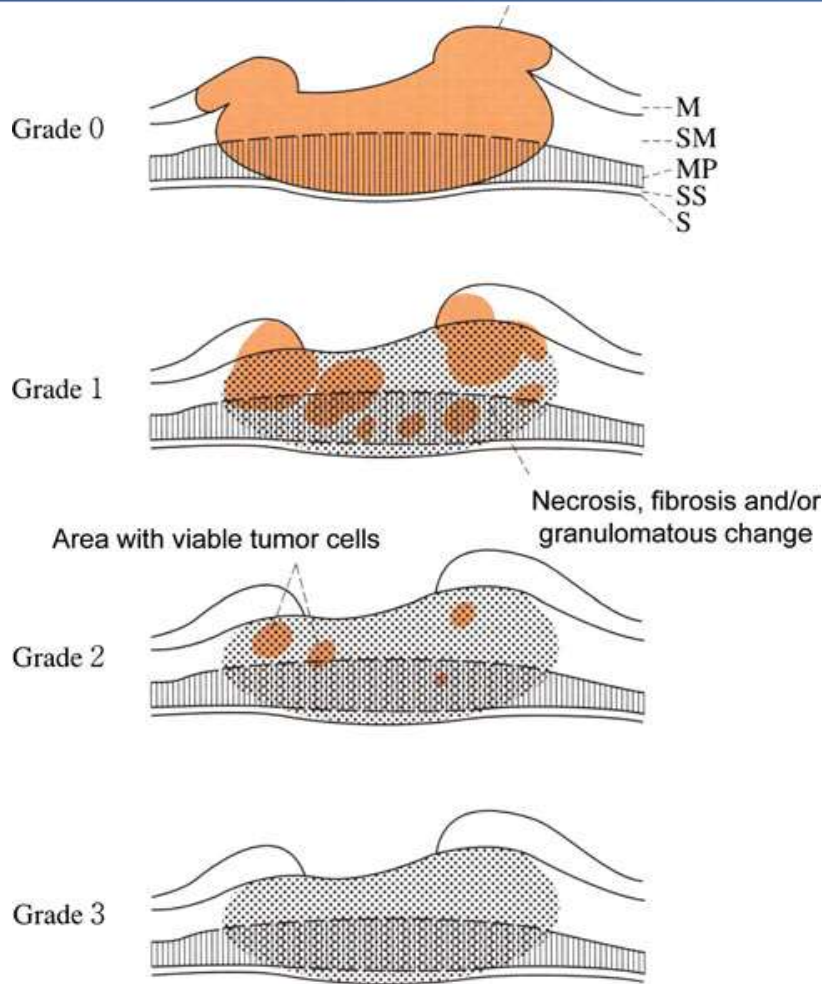


- 1) No residual tumor  
(complete regression of tumor).
- 2) Ulceration
- 3) No tumor metastasis, regional lymph nodes (0/30)

**Final Staging pT0N0M0**



# Histological evaluation criteria of tumor response after preoperative therapy



Grade 0 (no effect)

No evidence of effect

Grade 1 (slight effect)

Grade 1a

(very slight effect)

Viable tumor cells occupy more than 2/3 of the tumorous area

Grade 1b

(slight effect)

Viable tumor cells remain in more than 1/3 but less than 2/3 of the tumorous area

Grade 2

(considerable effect)

Viable tumor cells remain in less than 1/3 of the tumorous area

Grade 3

(complete response)

No viable tumor cells remain. It is recommended that the finding is confirmed on additional sectioning.



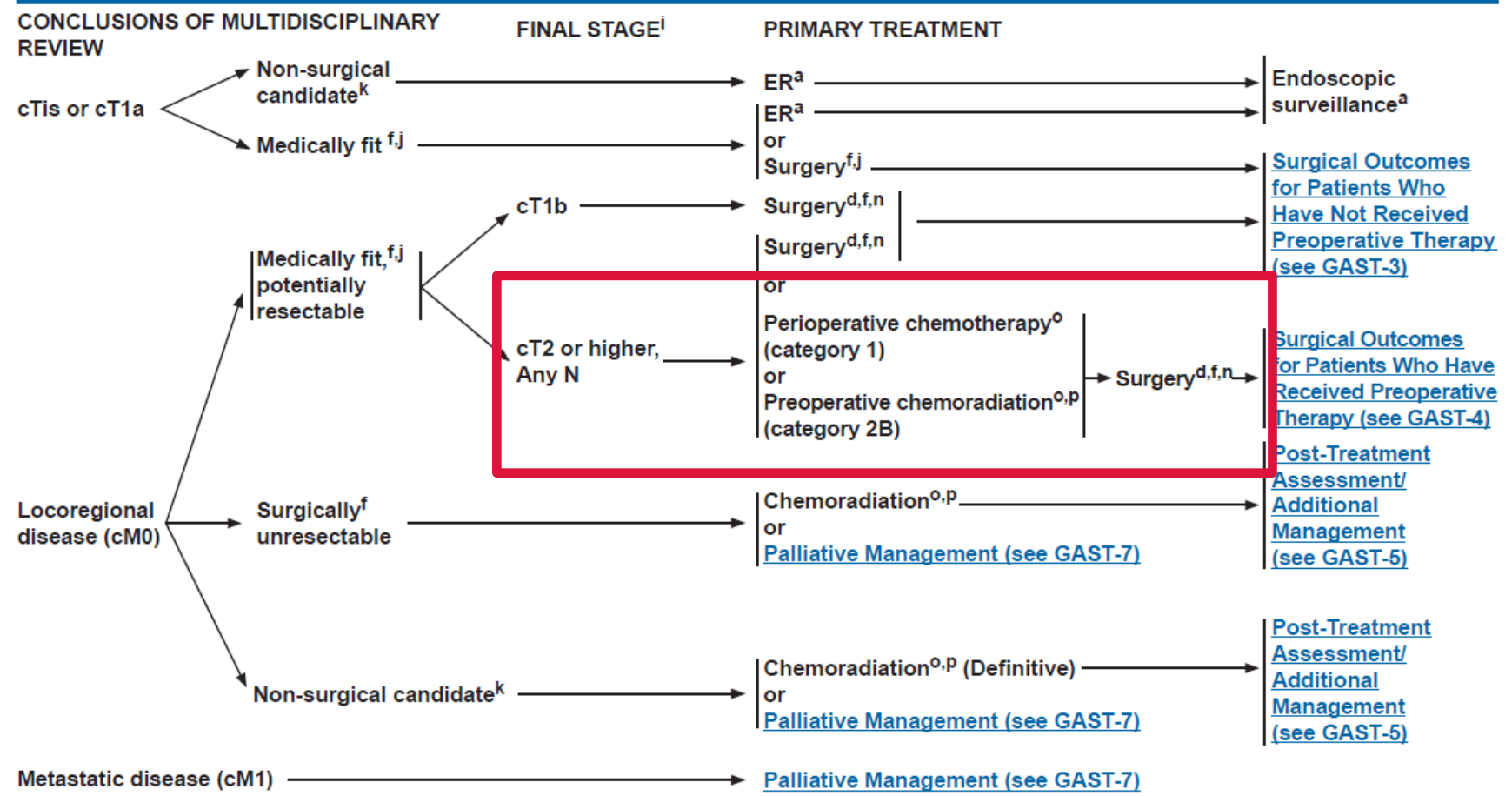
# Recommendations by NCCN



National  
Comprehensive  
Cancer  
Network®

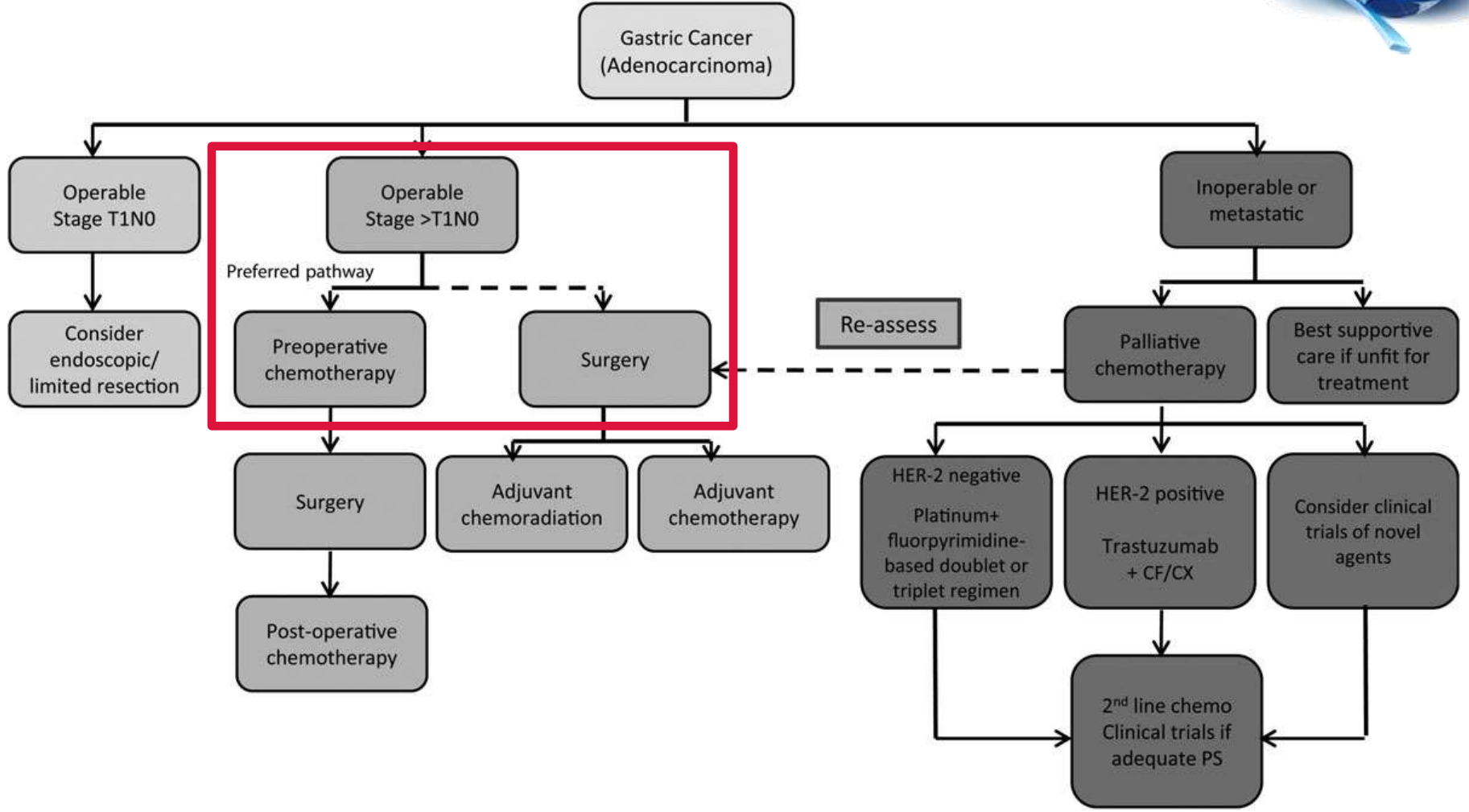
## NCCN Guidelines Version 1.2017 Gastric Cancer

[NCCN Guidelines Index](#)  
[Table of Contents](#)  
[Discussion](#)

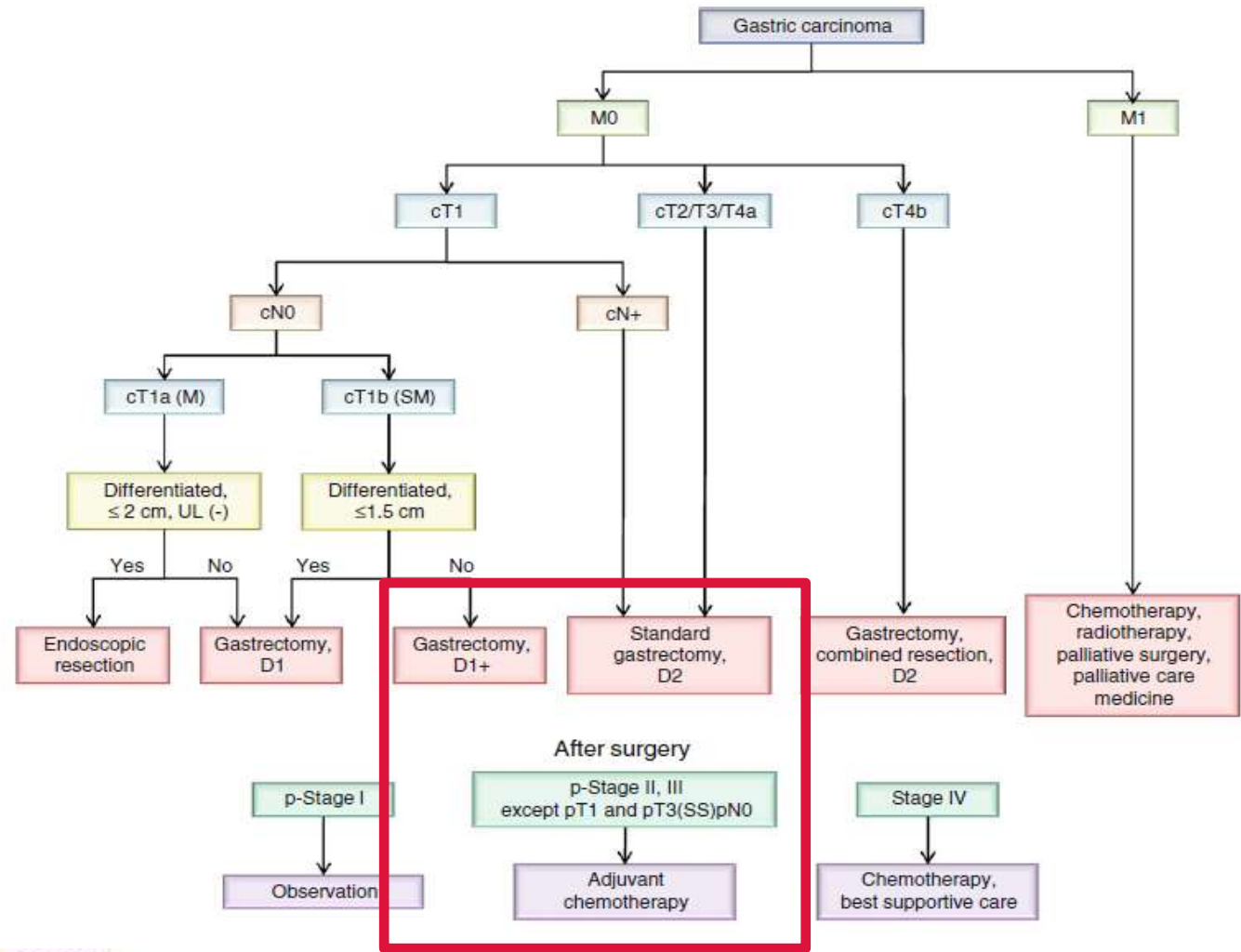




# Recommendations by ESMO-ESSO-ESTRO



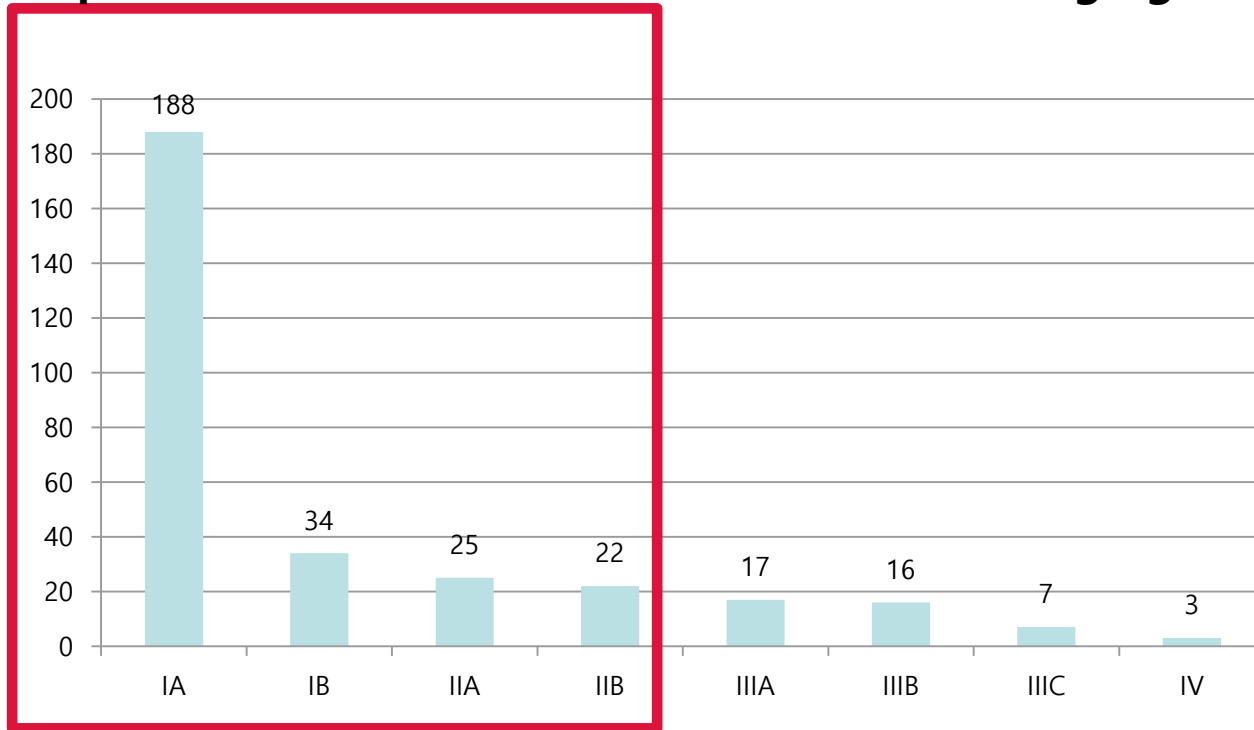
# Recommendation by Japanese Gastric Cancer Association



# Stomach Cancer Stage After Surgery; 2015 in the CNUH

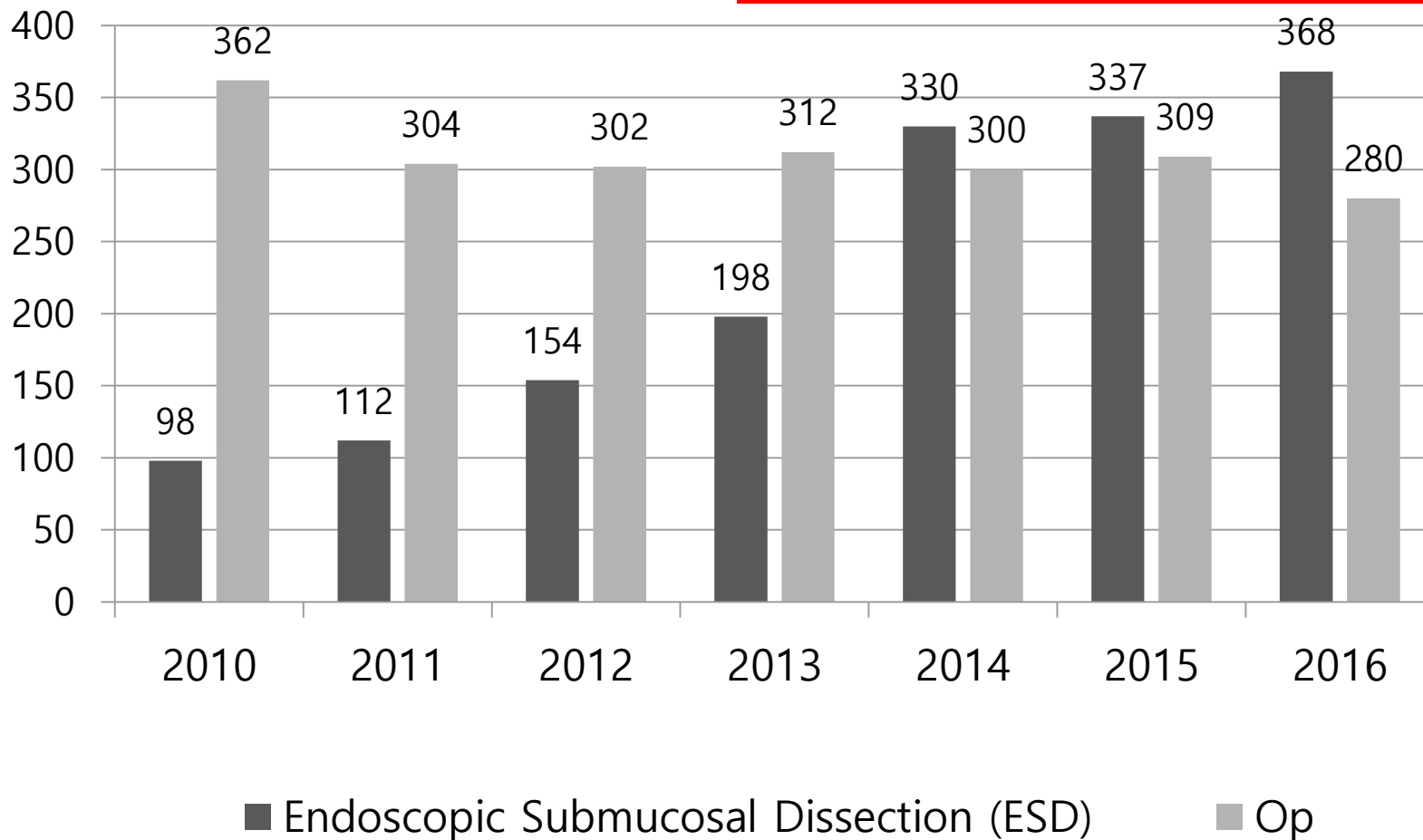


owing to national screening programs gastric cancer tends to be diagnosed earlier in Asian countries compared to countries in the western hemisphere so that there is no need for downstaging in most cases





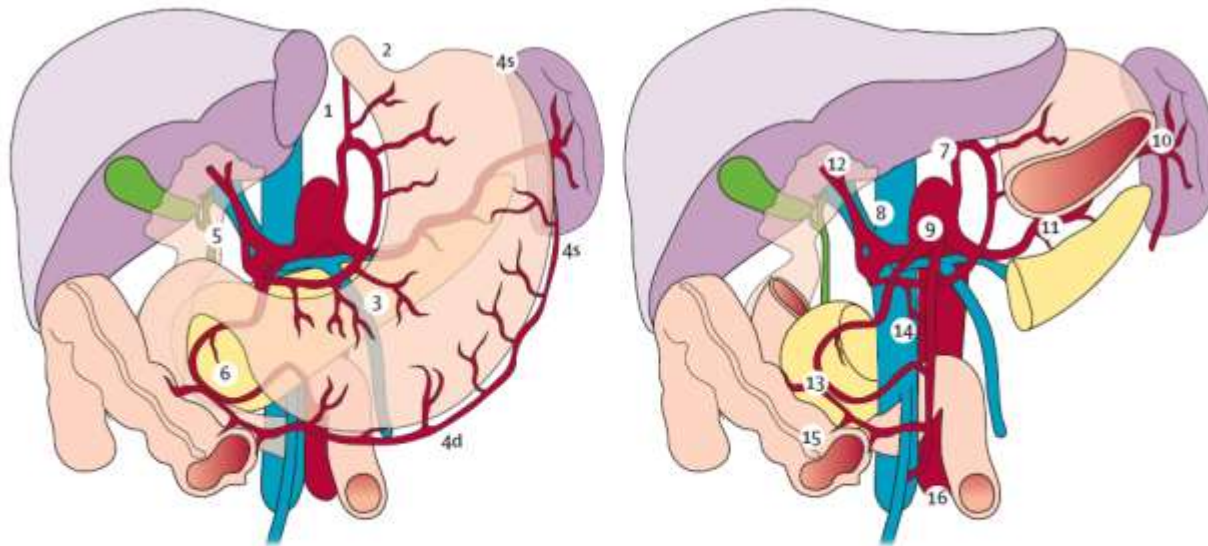
## Endoscopic vs Surgery in the CNUH





# Gastric cancer in the East and the West

- Standard surgical procedure
  - **Extended LN dissection (D2 dissection)** has been regarded as the standard, in Korea and Japan, traditionally.
  - In the US and Europe, perigastric LN dissection (D1 dissection) is still widely used.



N1 Lymph nodes (perigastric)

- 1 Right cardiac nodes
- 2 Left cardiac nodes
- 3 Nodes along the lesser curvature
- 4d Lymph nodes along the short gastric and the left gastroepiploic vessels
- 4s Lymph nodes along the right

N2 Lymph nodes (branches coeliac axis)

- 7 Nodes along root left gastric artery
- 8 Nodes along common hepatic artery
- 9 Nodes around coeliac axis
- 10 Nodes at splenic hilum
- 11 Nodes along splenic artery

N3 Lymph nodes

- 12 Nodes at the hepatoduodenal ligament
- 13 Retropancreatic (periduodenal) nodes
- 14 Nodes at the root of the mesentery

N4 Lymph nodes

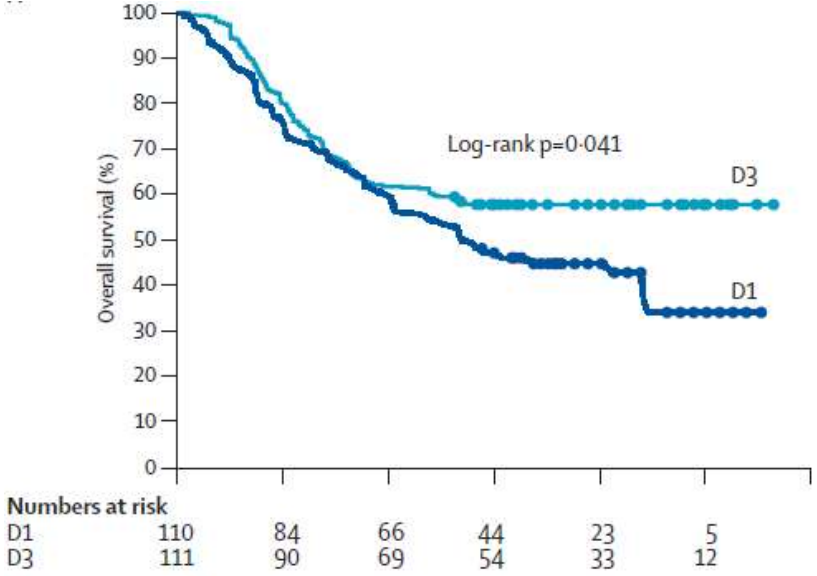
- 15 Nodes along the middle colic vein
- 16 Para-aortic nodes



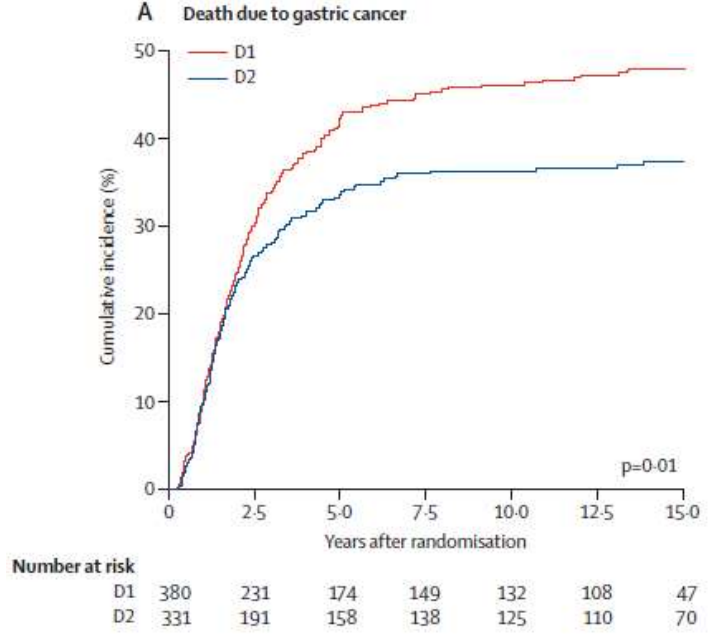
# Gastric cancer in the East and the West



- Comparison of surgical procedures, D1 vs D2



Wu CW, et al.  
Lancet Oncol 2006; 7: 309



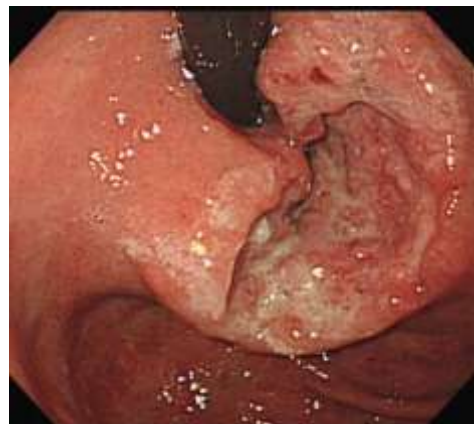
Songun I, et al.  
Lancet Oncol 2010; 11: 439

- **D2 dissection** should be recommended as the standard, if performed safely by experienced surgeons

# Gastric cancer in the East and the West



- Another difference between the East and the West most probably lies in the tumor biology, which seems also to be reflected by the tumor location. While the incidence of adenocarcinoma of the **lower esophagus and the gastric cardia (AEG I~III) is increasing in most Western populations**
- **in Asian countries** where gastric carcinoma in the proper sense is more common junctional adenocarcinomas are **still rare**



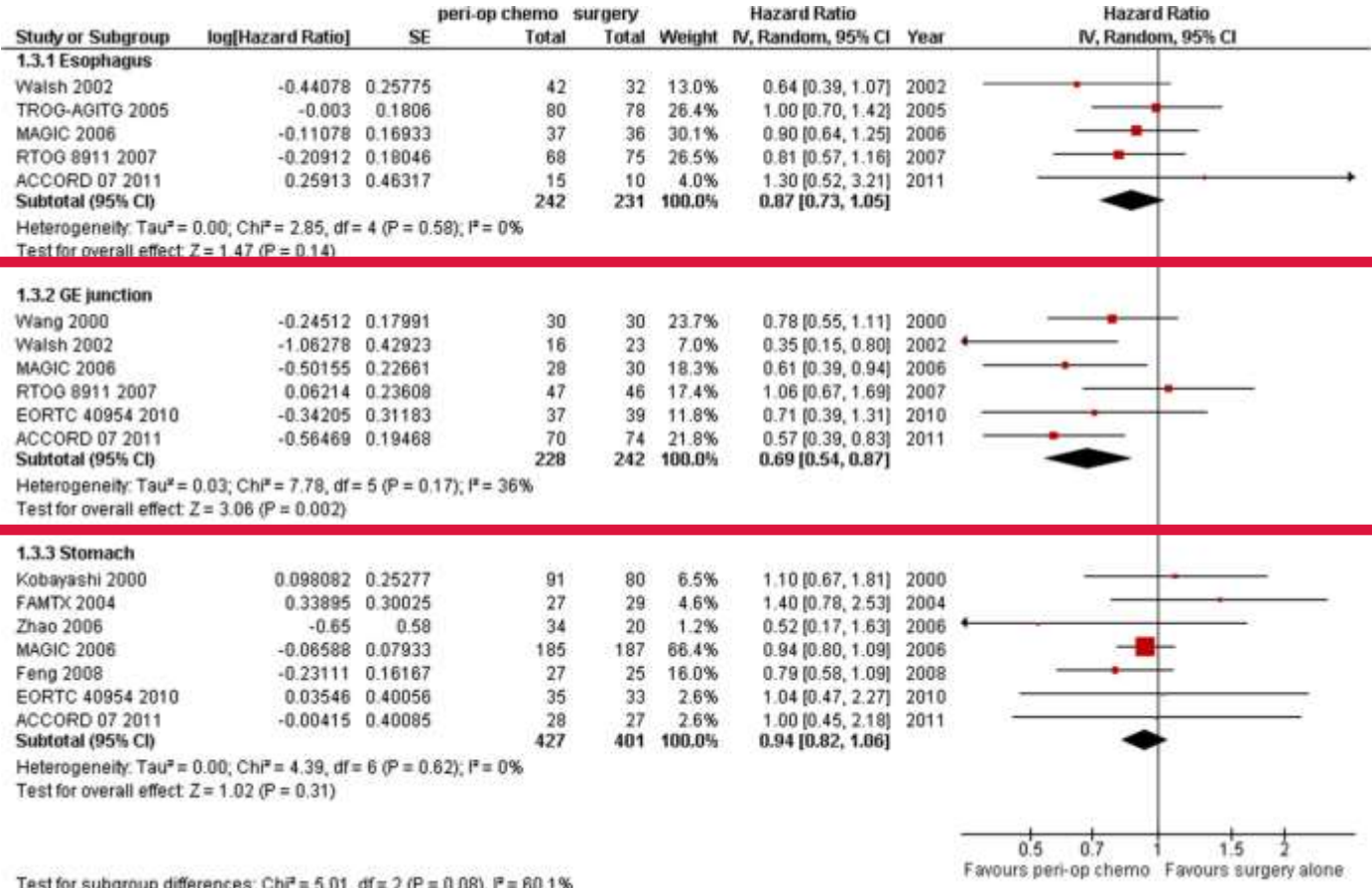
**VS**





# Gastric cancer in the East and the West

## Overall survival by tumour site

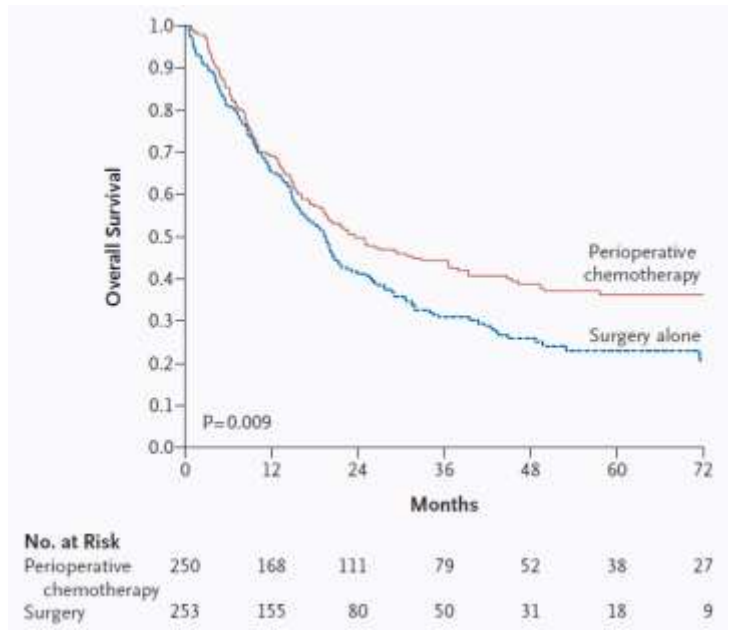
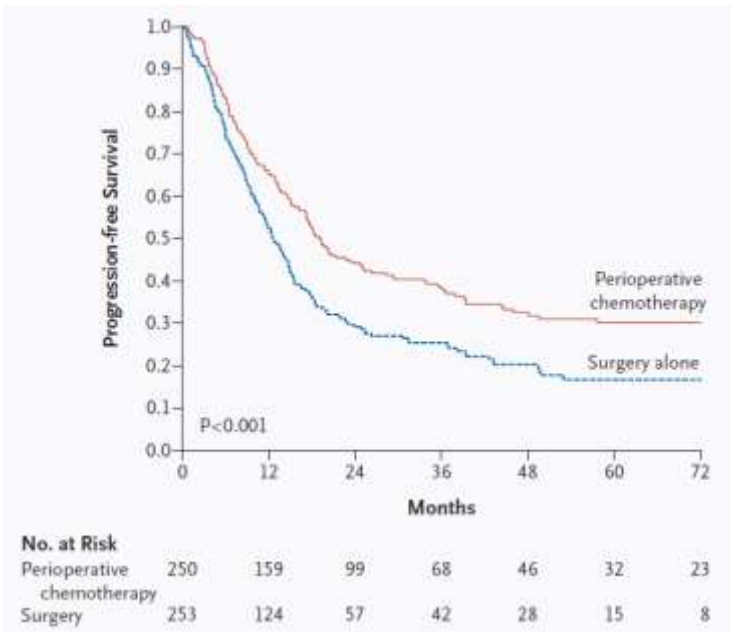
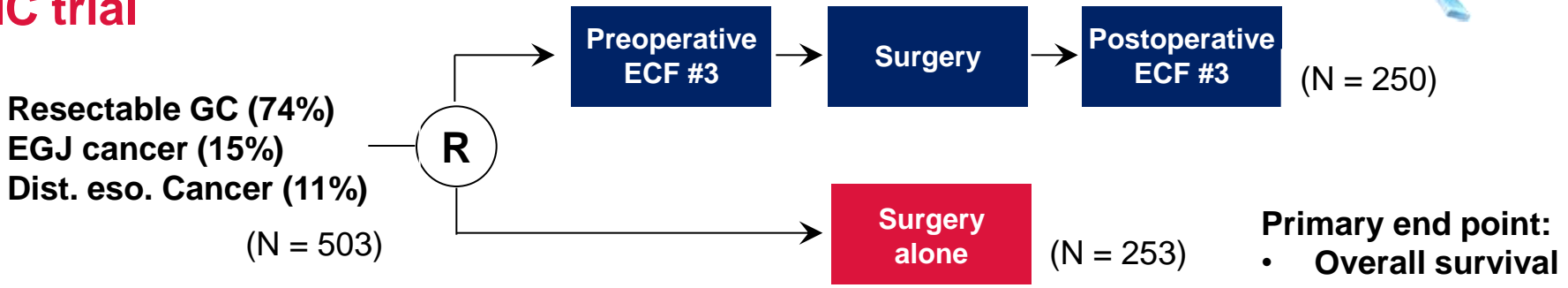


Test for subgroup differences: Chi<sup>2</sup> = 5.01, df = 2 (P = 0.08), I<sup>2</sup> = 60.1%



# Evidences of preoperative chemotherapy

## MAGIC trial



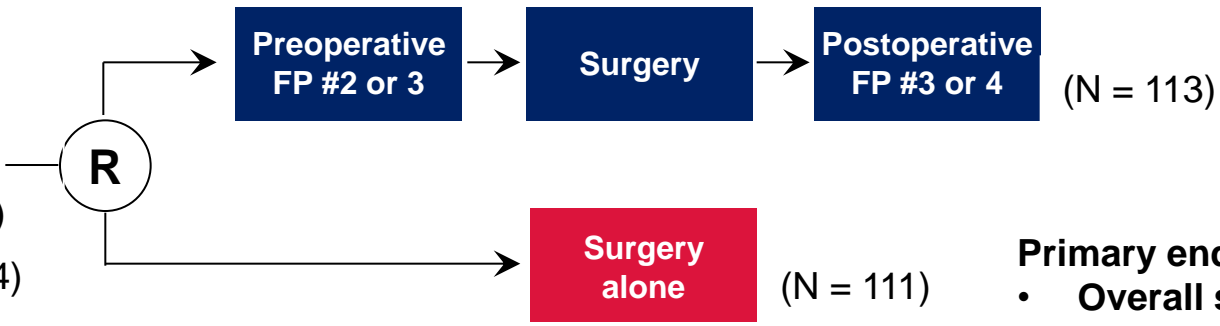


# Evidences of preoperative chemotherapy

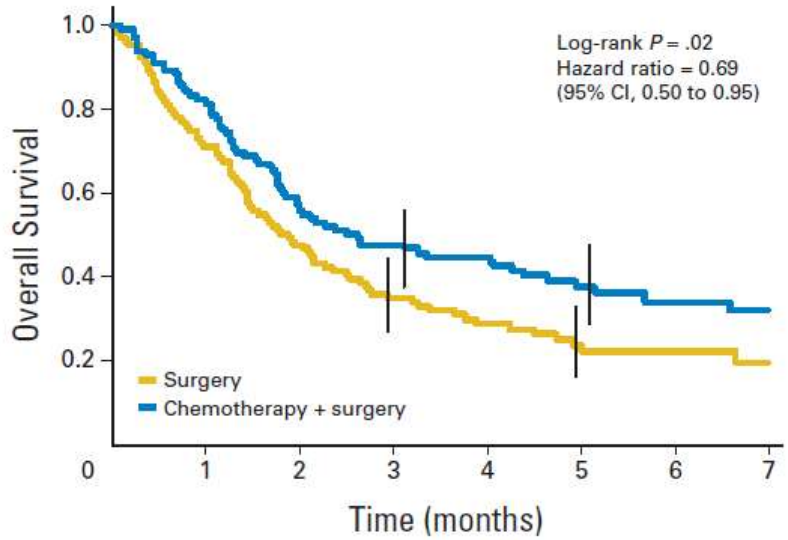


## FNCLCC-FFCD trial

Resectable GC (25%)  
EGJ cancer (64%)  
Dist. eso. Cancer (11%)  
(N = 224)



Primary end point:  
• Overall survival

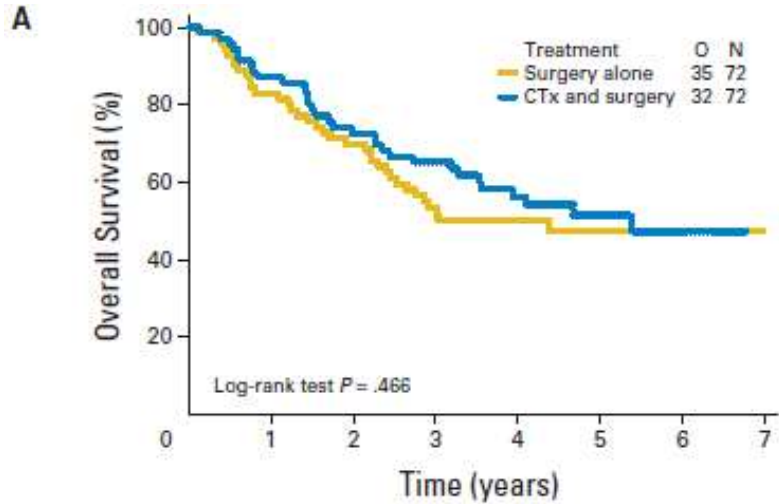
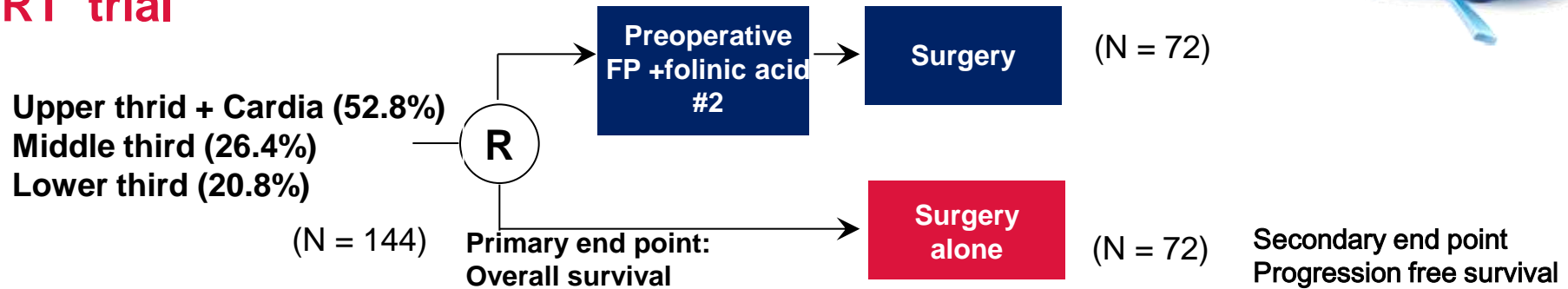


No. at risk	0	1	2	3	4	5	6	7
Surgery	111	79	53	38	27	16	13	7
Chemotherapy + surgery	113	93	65	53	41	27	17	14

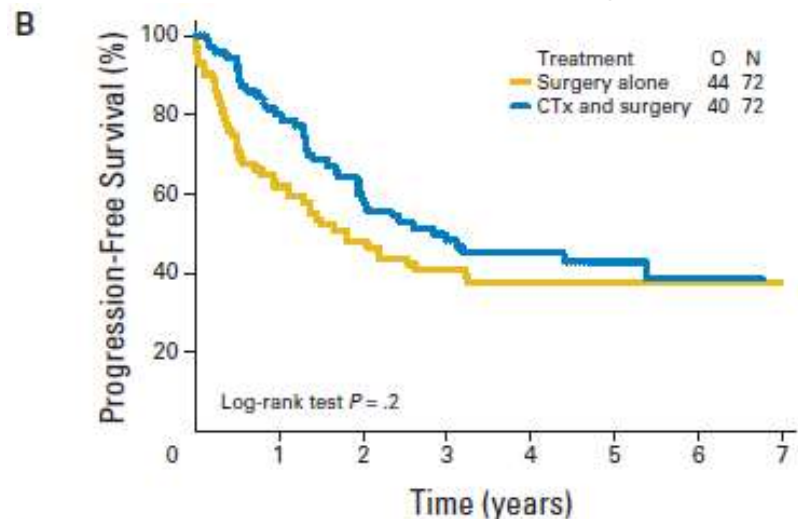


# Evidences of preoperative chemotherapy

## EORTC trial



No. at risk	0	1	2	3	4	5	6	7
Surgery alone	58	48	34	20	11	4		
CTx and surgery	61	49	41	29	15	6		



No. at risk	0	1	2	3	4	5	6	7
Surgery alone	44	34	28	16	11	4		
CTx and surgery	56	41	31	24	13	5		

# Possible disadvantages of Neoadjuvant Treatment



- Patients with resectable cancer **may miss the opportunity for a curative gastrectomy** if their disease progresses during pre-operative therapy
- Patients with early gastric carcinoma (stages 0 and I) could be **over-treated**, and among the stages II-IV non-metastatic gastric cancers, the response to the preoperative therapy could be **unsatisfactory**
- **Definitive surgery may be delayed or surgical morbidity increased** owing to toxicity associated with neoadjuvant treatment
- **Assessment of pathologic stage is limited** in the setting of preoperative therapy, resulting in the potential loss of important prognostic information.

# Theoretical basis of preoperative chemotherapy



## *Still attractive because ...*

- Chemotherapy delivery may be more efficient if given prior to **surgical disruption of the vasculature**.
- Owing to a usually better preoperative general health condition of patients the **full chemotherapy-dosage can be applied**
- **Reduction of contamination of the abdominal cavity** with tumor cells because of a 'sterilization' of the tumor

*Fugitani K. Dig Surg 2013; 30: 119*  
*Christoph S .J Gastric Cancer2013;13:73*



# Theoretical basis of preoperative chemotherapy



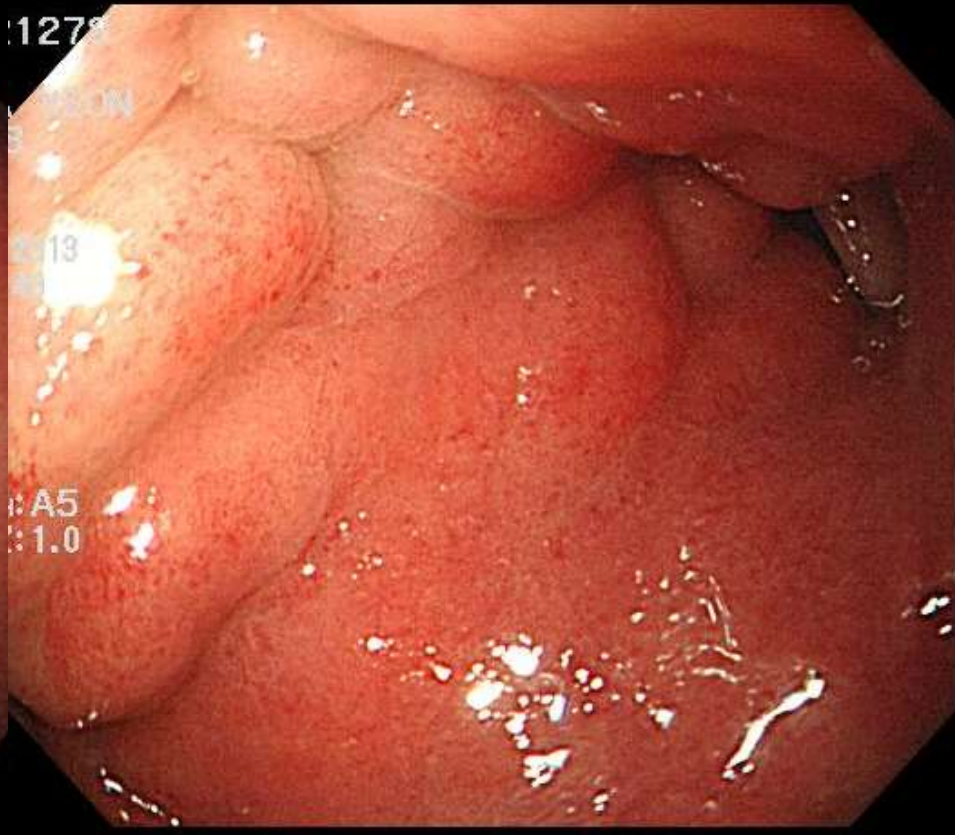
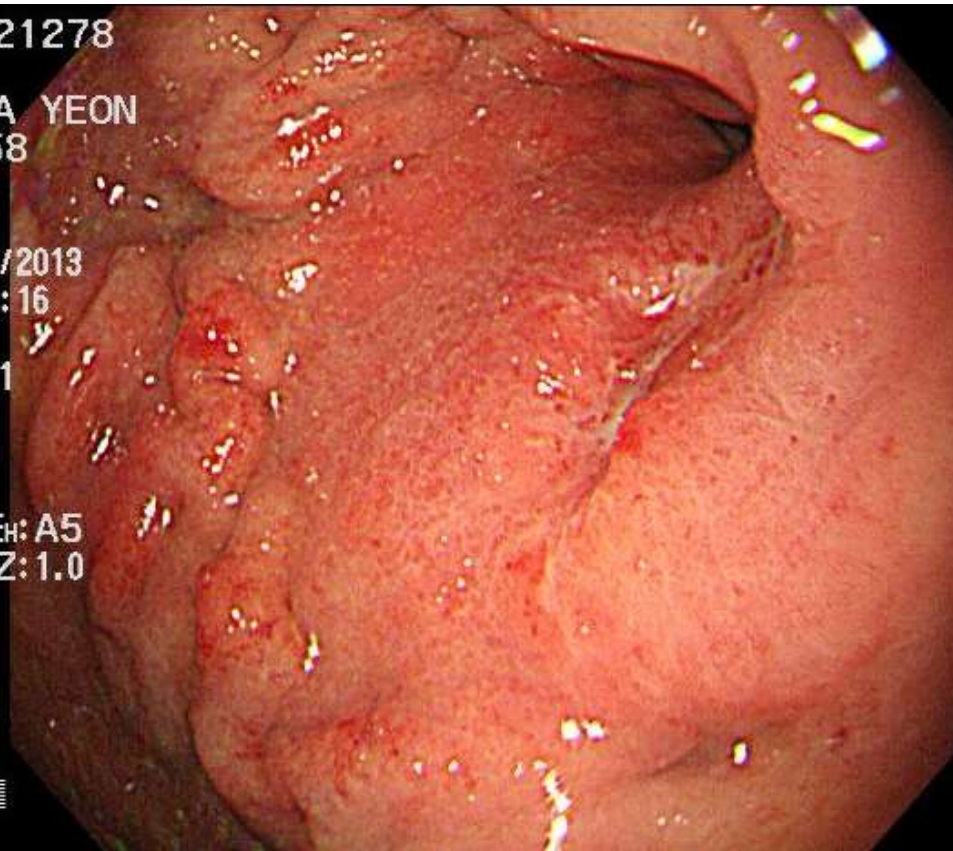
*Still attractive because ..*

- Neoadjuvant chemotherapy is the earliest means of **eliminating systemic micrometastases**.
- Neoadjuvant therapy potentially leads to **downsizing** or **downstaging** of the tumor and may therefore substantially facilitate its complete resection.
- Neoadjuvant chemotherapy can be used to assess tumor **chemosensitivity** to cytotoxic medications.

*Fugitani K. Dig Surg 2013; 30: 119*

*Christoph S .J Gastric Cancer2013;13:73*

58/M

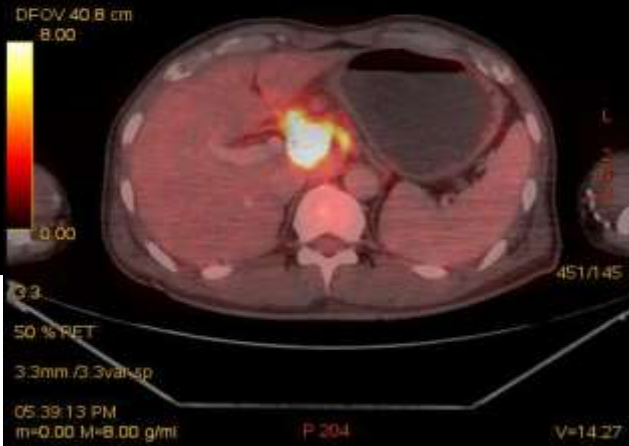


# 58/M

## Initial cStaging [T4aN2M0, IIB]



Axial Volume 2/Volume 1  
Ex: 50% 22560 / 50% 22560  
A 204  
SO BYEONG CHEOL  
CHUNGNAMUNIVERSITYHOSPITAL  
M 52 01420029  
DoB: Sep 04 1961  
Ex: Dec 18 2013





# NAC regimen & schedule



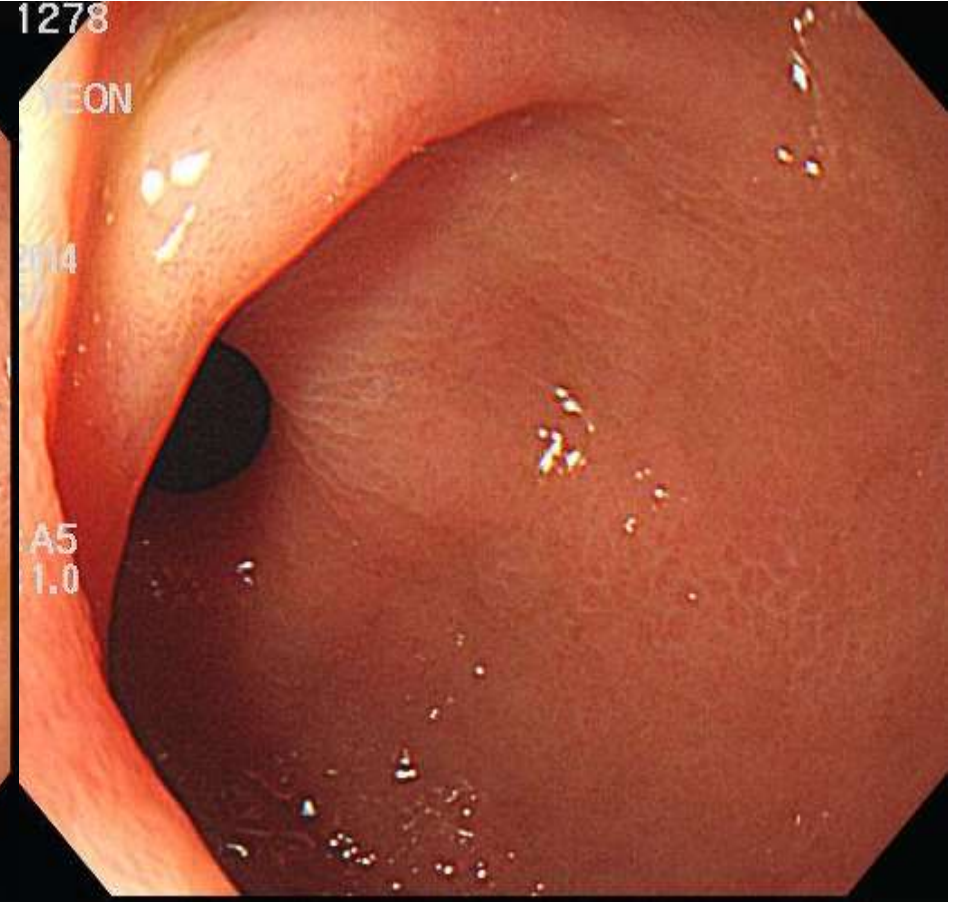
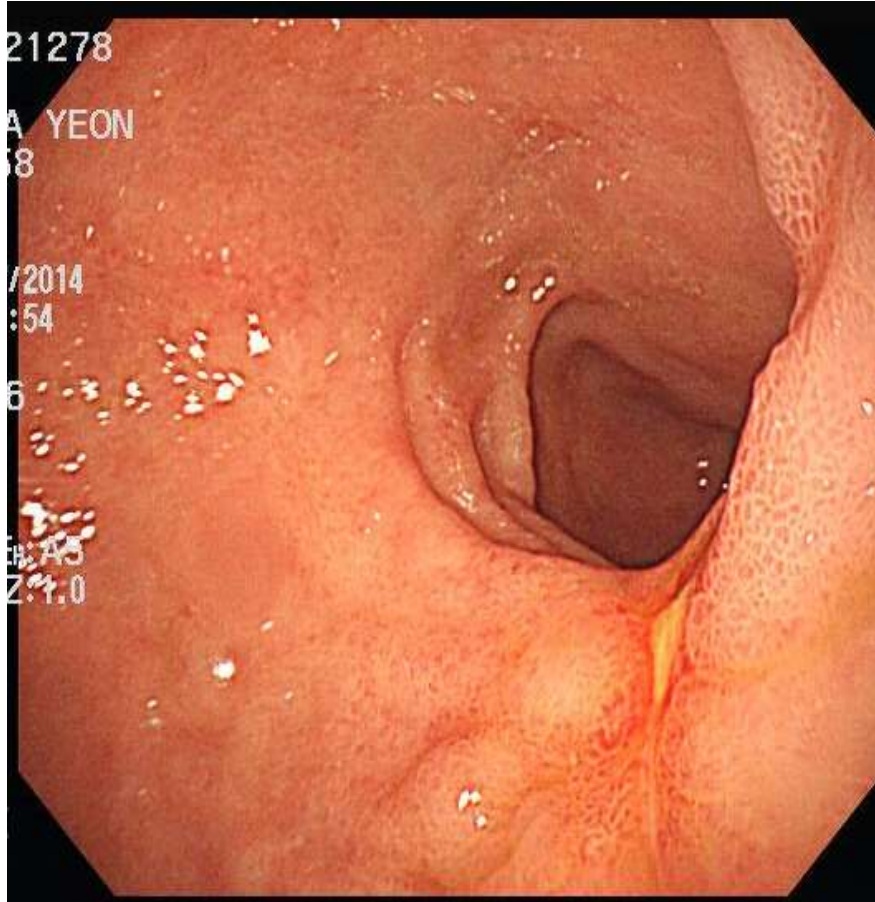
Regimen	Dose	Duration
5-FU	2400mg/m <sup>2</sup>	D1 (H2-48)
Oxaliplatin	100mg/m <sup>2</sup>	D1 (H0-2)

Every 2 weeks for three cycles.

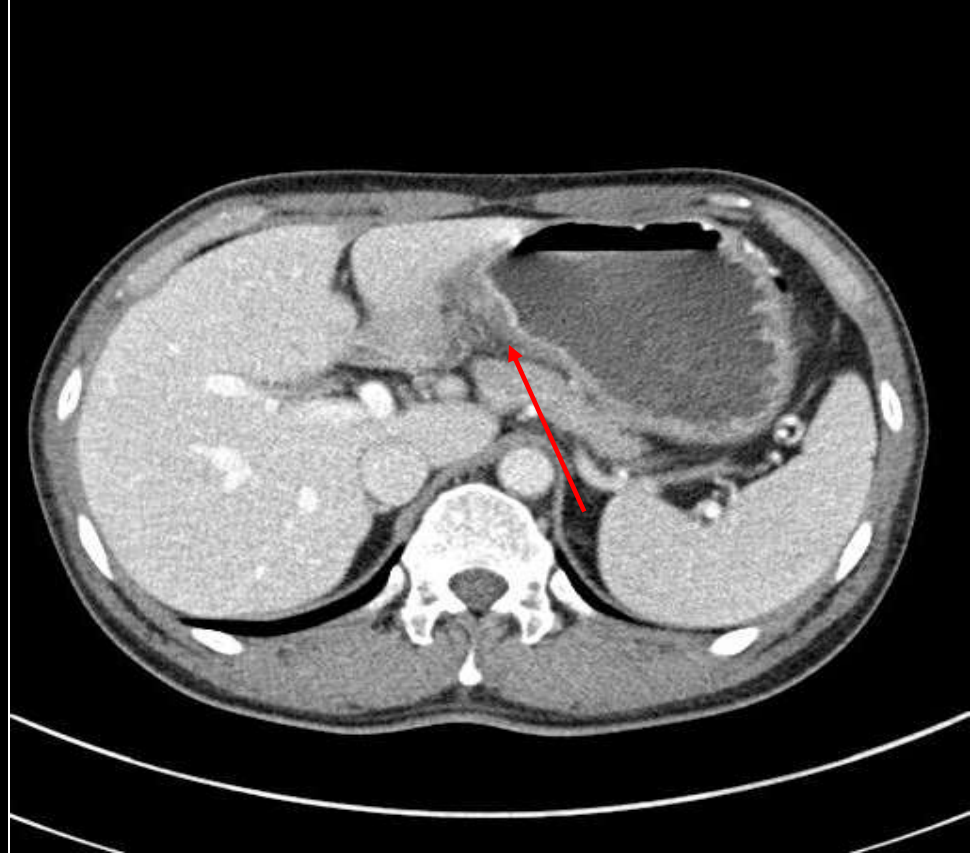
- 2013.12.27~ 12.29) #1. FOLFOX
- 2014.01.11~ 01.13) #2. FOLFOX
- 2014.01.25~ 01.27) #3. FOLFOX



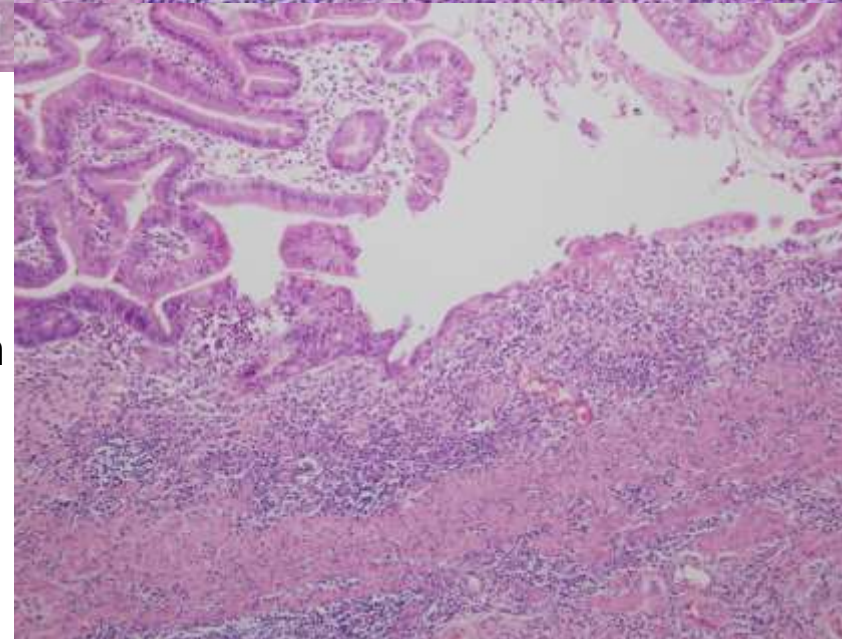
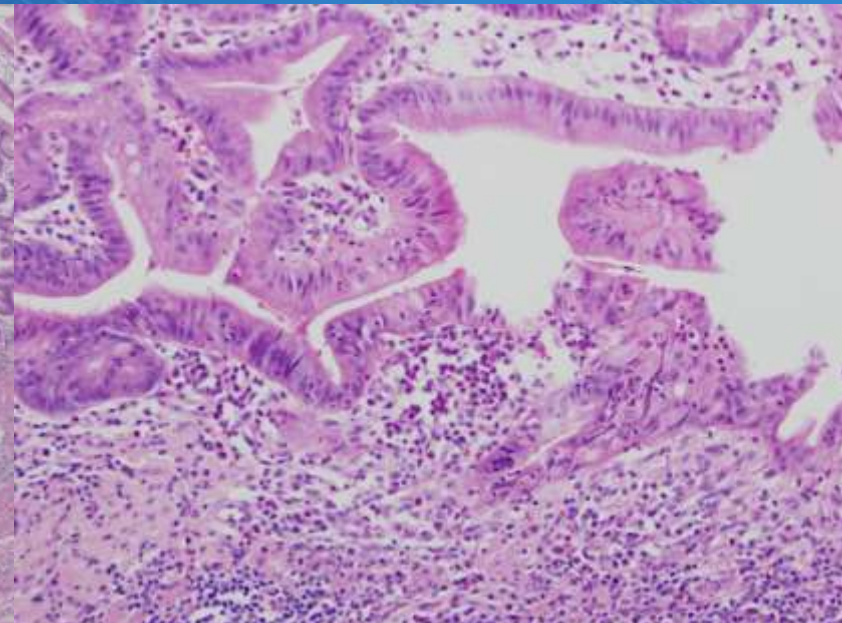
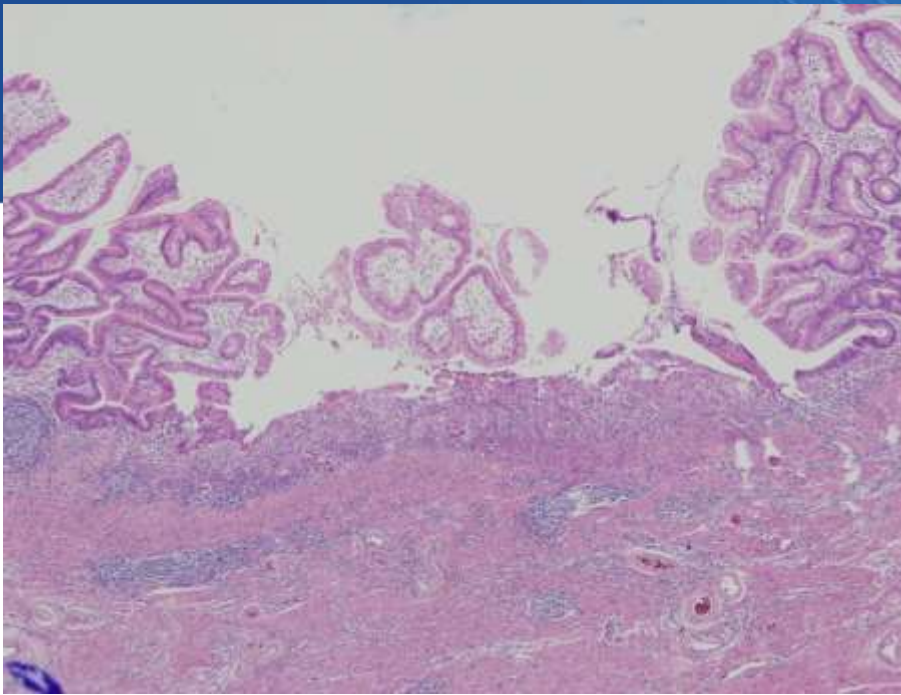
# After Neoadjuvant Treatment



# After Neoadjuvant Treatment







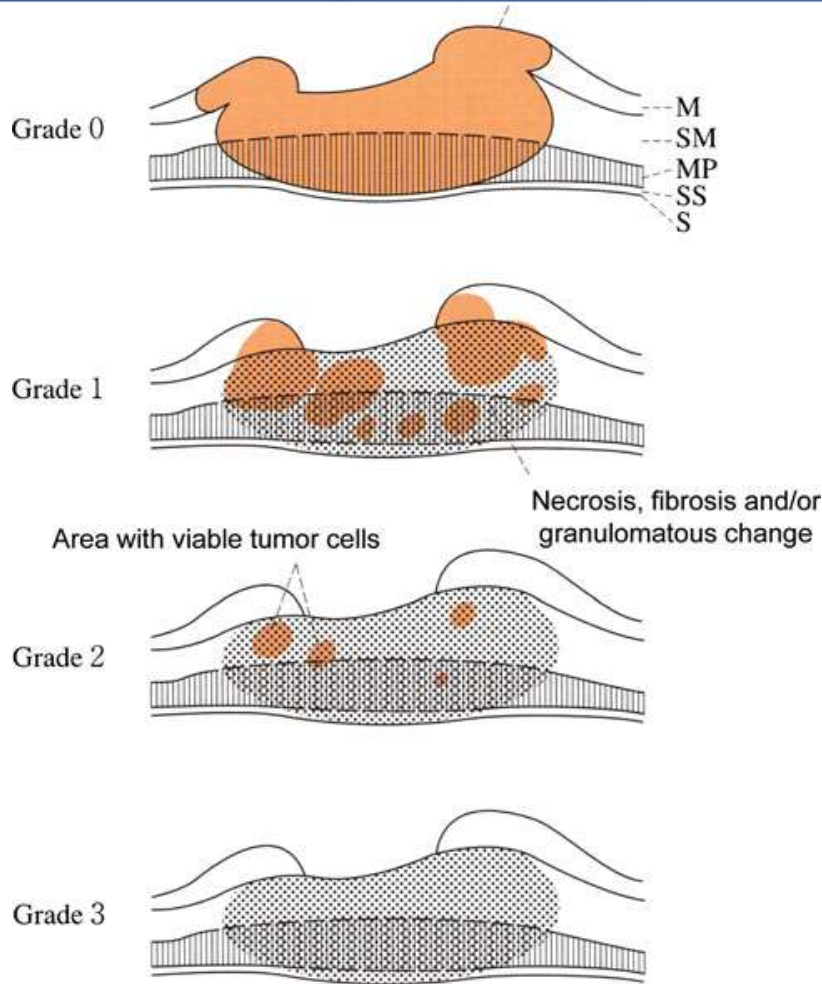
- 1) tumor size: 0.3x0.2cm
- 2) histologic type: tubular adenocarcinoma
- 3) Lauren classification: intestinal type
- 4) differentiation: well
- 5) depth of invasion: invades lamina propria

or muscularis mucosae (pT1a)

- 6) lymphovascular invasion: absent
- 7) perineural invasion: absent
- 8) lymph node metastasis : absent (0/49)

**Final Stage IA pT1aN0M0**

# Histological evaluation criteria of tumor response after preoperative therapy



Grade 0 (no effect)

No evidence of effect

Grade 1 (slight effect)

Grade 1a  
(very slight effect)

Viable tumor cells occupy more than 2/3 of the tumorous area

Grade 1b  
(slight effect)

Viable tumor cells remain in more than 1/3 but less than 2/3 of the tumorous area

Grade 2  
(considerable effect)

Viable tumor cells remain in less than 1/3 of the tumorous area

Grade 3  
(complete response)

No viable tumor cells remain. It is recommended that the finding is confirmed on additional sectioning.



# Retrospective date in the CNUH (2008~2014); 41 명 NAC 환자 분석



## Stage Change of the Pretreatment *vs.* Post Neoadjuvant Chemotherapy

Characteristic	Pretreatment (clinical stage)	Post NAC (pathologic stage)	p-value
Tumor stage			0.000
T1	0 (0)	6 (14.6)	
T2	1 (2.4)	4 (9.8)	
T3	13 (31.7)	3 (7.3)	
T4	27 (65.9)	28 (68.3)	
Nodal status			0.000
N0	1 (2.4)	12 (29.3)	
N1	2 (4.9)	8 (19.5)	
N2	26 (63.4)	5 (12.2)	
N3	12 (29.3)	16 (39.1)	
Change of overall stage			
Downstage		21 (51.2)	
Upstage		9 (22.0)	
No change		11 (26.8)	

# Retrospective date in the CNUH (2008~2014)



Characteristic	NAC group (n=41)	Surgery only group (n=342)	p-value
Type of surgery			0.726
Total gastrectomy	6 (14.6)	39 (11.4)	
Distal gastrectomy	35 (85.4)	303 (88.6)	
Resection margin			0.829
R0	38 (92.7)	321 (93.9)	
R1	2 (4.9)	20 (5.8)	
R2	0 (0)	1 (0.3)	
Open & closure	1 (2.4)	0 (0)	
Postoperative complication	6 (14.6)	61 (17.8)	0.770
Pathologic results			
Tumor stage			0.001
T1	6 (14.6)	0 (0)	
T2	4 (9.8)	8 (2.3)	
T3	3 (7.3)	128 (37.4)	
T4	28 (68.3)	206 (60.2)	
Nodal status			0.000
N0	12 (29.3)	4 (1.2)	
N1	8 (19.5)	72 (21.1)	
N2	5 (12.2)	96 (28.1)	
N3	16 (39.0)	170 (49.7)	
Metastasis status			0.127
M0	39 (95.1)	338 (98.8)	
M1	2 (4.9)	4 (1.2)	

# Retrospective date in the CNUH (2008~2014)



## Grade 3 or 4 Toxicity and Clinical Response Assessment during Neoadjuvant Chemotherapy

Variable	Total (n=41)	Doublet (n=28)	Triplet (n=13)	p-value
Toxicity (total)	15 (36.6)	9 (32.1)	6 (46.2)	0.604
Neutropenia	5 (12.2)	4 (14.3)	1 (7.7)	
Thrombocytopenia	3 (7.3)	1 (3.6)	2 (15.4)	
Anemia	2 (4.9)	1 (3.6)	1 (7.7)	
Nausea/vomiting	2 (4.9)	2 (7.1)	0 (0)	
Mucositis	1 (2.4)	0 (0)	1 (7.7)	
Fever	1 (2.4)	0 (0)	1 (7.7)	
Nephrotoxicity	1 (2.4)	1 (3.6)	0 (0)	
Clinical response				0.374
Complete response	5 (12.2)	3 (10.7)	2 (15.4)	
Partial response	14 (34.1)	9 (32.1)	5 (38.5)	
Stable disease	19 (46.3)	15 (53.6)	4 (30.8)	
Progressive disease	3 (7.3)	1 (3.6)	2 (15.4)	

# Results of phase III pre- or perioperative chemotherapy trials in gastric and GE junction cancer



Study	Treatment	No. of patients	R0 resection rate (%)	Pathologic CR rate	Survival		Local failure*
					Median	Overall	
Cunningham et al.	Periop ECF+surgery	250	69	0%	24 months	5-year 36%	14%
	Surgery	253	66	N/A	20 months	5-year 23%	21%
Ychou et al.	Periop 5FU/Cis+surgery	109	87	NS	NS	5-year 38%	24%
	Surgery	110	74	N/A	NS	5-year 24%	26%
Schumacher et al.	Preop 5FU/LV/Cis +surgery	72	82	7.1%	64.6 months	2-year 73%	NS
	Surgery	72	67	N/A	52.5 months	2-year 70%	

*Cis* cisplatin, *CR* complete response, *ECF* epirubicin, cisplatin, 5-fluorouracil, *LV* leucovorin, *N/A* not applicable, *NS* not stated



# META-ANALYSIS & SYSTEMATIC REVIEW



	<b>Overall Survival (OS) rate</b>	<b>R 0 resection rate</b>
B. Xiong et al	1.32 (1.07-1.64) P=0.01	1.38 (1.08-1.78) P=0.01
Xu A-M et al	0.83 (0.65-1.06) P=0.14	1.02 (0.89-1.17) P=0.81
U. Ronellenfitsch et al	0.81 (0.73-0.89) p<0.0001	1.42 (0.97-2.06)
Y Liao et al	1.16 (0.85-1.58) P=0.36	1.24 (0.78-1.96) P=0.36
Lei Ge et al	1.40 (1.11-1.76) P=0.005	1.42 (1.01-2.02) P=0.05

# META-ANALYSIS & SYSTEMATIC REVIEW



	<b>Postoperative complication</b>
B. Xiong et al	0.57 (0.25-1.30) P=0.18 0.88 (0.41-1.91) P=0.75 1.27 (0.27-5.93) P=0.76
Xu A-M et al	1.14 (0.77-1.70) P=0.51
U. Ronellenfitsch et al	0.01 (0.03-0.05)
Y Liao et al	1.25 (0.75-2.09) P=0.39
Lei Ge et al	1.04 (0.56-1.93) P=0.91

Xu A-M et al. PLoS ONE 9(1): e86941

B. Xiong et al. EJSO 40 (2014) 1321-1330

U. Ronellenfitsch et al. European Journal of Cancer 49 (2013) 3149–3158

Ge L et al *World J Gastroenterol* 2012 18(48): 7384-7393

Y.Lia et al. Journal of Gastroenterology and Hepatology 28 (2013) 777–782

# Phase II for marginally/potentially resectable cases



	JCOG 0210 trial	JCOG 0001 trial	JCOG 0405 trial
<b>Target disease</b>	<b>Large Borrmann III Borrmann IV</b>	<b>Paraaortic LN Bulky nodal diseases</b>	<b>Paraaortic LN Bulky nodal diseases</b>
Regimen	S-1 + Cisplatin	Irinotecan + Cisplatin	S-1 + Cisplatin
Cycles	2	2 - 3	2 – 3
Enrolled patients, n	50	55	51
Response rate, %	Not reported	55	63
R0 resection rate, %	73	65	82
ypCR rate, %	2	0	2
3-year OS rate, %	26	27	59

# Phase III for marginally/potentially resectable cases



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## A Trial of Neoadjuvant TS-1 and Cisplatin for Type 4 and Large Type 3 Gastric Cancer

**This study is currently recruiting participants.**

*Verified June 2010 by Japan Clinical Oncology Group*

**Sponsor:**

Japan Clinical Oncology Group

**Collaborator:**

Ministry of Health, Labour and Welfare, Japan

**Information provided by:**

Japan Clinical Oncology Group

ClinicalTrials.gov Identifier:

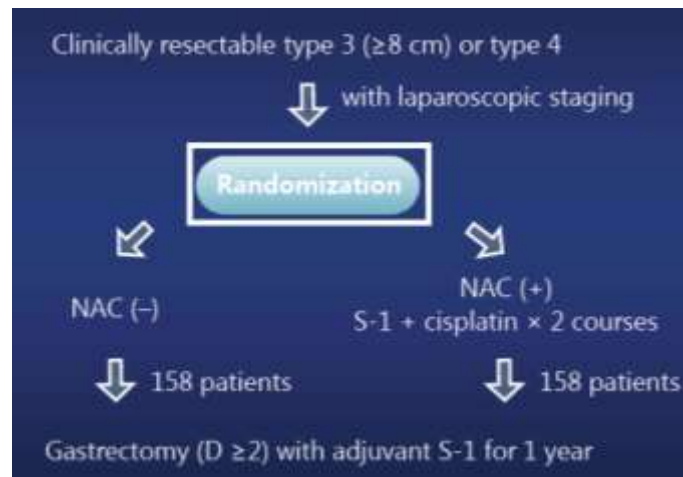
NCT00252161

First received: November 10, 2005

Last updated: June 13, 2010

Last verified: June 2010

[History of Changes](#)



**Primary end point:**

- Overall survival



# Current studies for the role of neoadjuvant therapy



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## Docetaxel+Oxaliplatin+S-1 (DOS) Regimen as Neoadjuvant Chemotherapy in Advanced Gastric Cancer (PRODIGY)

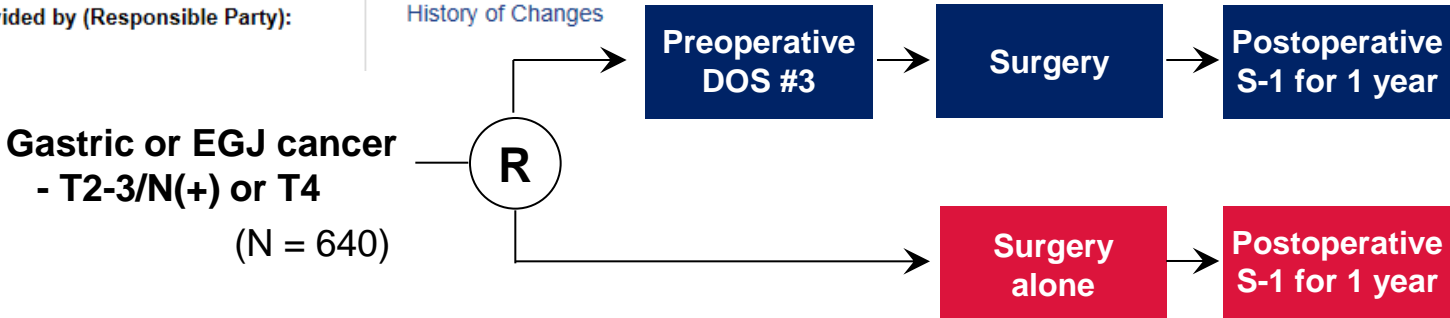
This study is currently recruiting participants.

Verified November 2013 by Sanofi

Sponsor:  
Sanofi

Information provided by (Responsible Party):  
Sanofi

ClinicalTrials.gov Identifier:  
NCT01515748  
First received: January 10, 2012  
Last updated: November 26, 2013  
Last verified: November 2013  
[History of Changes](#)



Primary end point:  
• Progression-free survival

Secondary end point:  
• Overall survival  
• yp stage and R0 resection rate

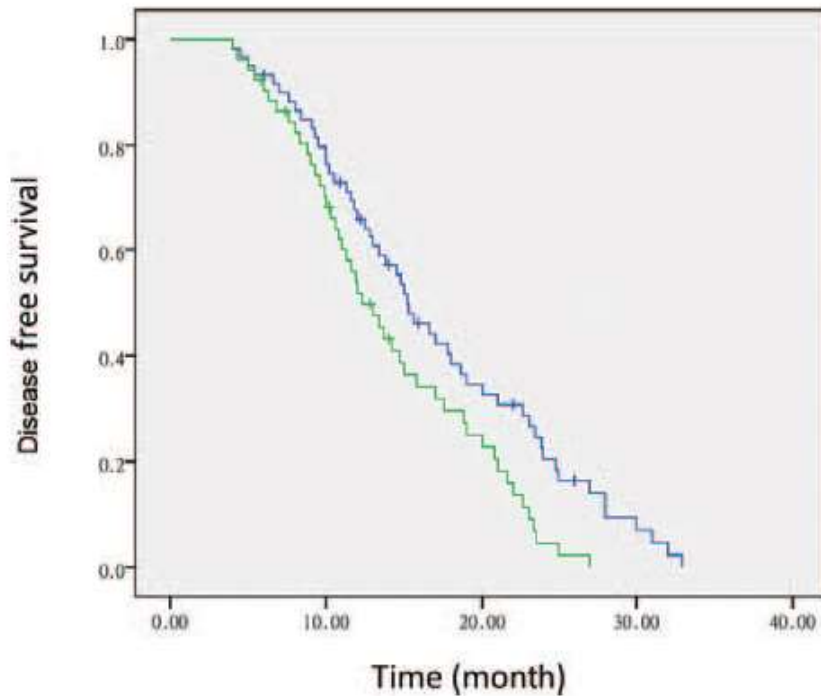


# Neoadjuvant Therapy of DOF Regimen Plus Bevacizumab Can Increase Surgical Resection Rate in Locally Advanced Gastric Cancer A Randomized, Controlled Study

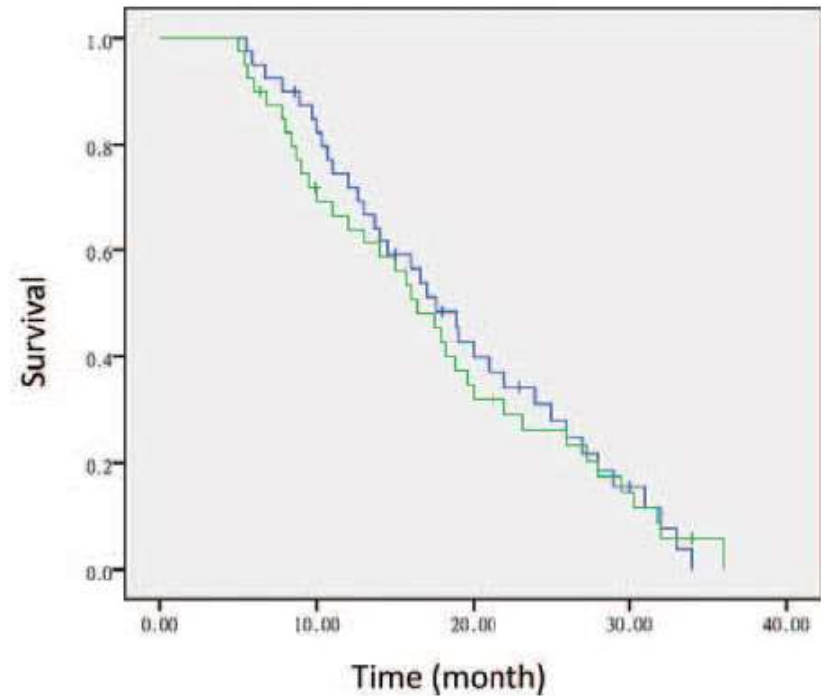
	DOF Group (n = 40)	DOF Plus Bevacizumab Group (n = 40)
Complete remission (n, %)	2 (5%)	4 (10%)
Partial remission (n, %)	15 (37.5%)	22 (55%)
Stable disease (n, %)	17 (42.5%)	12 (30%)
Disease progression (n, %)	6 (15%)	2 (5%)

	DOF Group (n = 40)	DOF Plus Bevacizumab Group (n = 40)	P Value
D2 resection (n)	22	31	0.0191
R0 resection (n)	20	30	0.0209
Debulking surgery (n)	9	4	0.1297
Palliative surgery	6	3	0.2885
Unresectable	4	2	0.3959
Positive surgical margin	5	2	0.2352

# Neoadjuvant Therapy of DOF Regimen Plus Bevacizumab Can Increase Surgical Resection Rate in Locally Advanced Gastric Cancer A Randomized, Controlled Study



**P = 0.013**

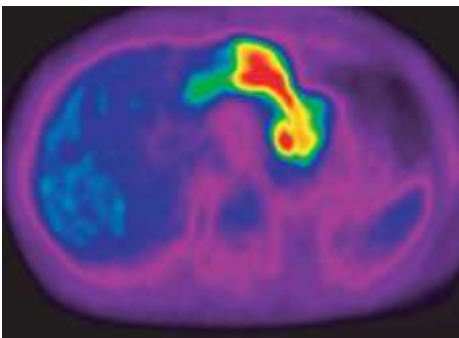


**P = 0.776**

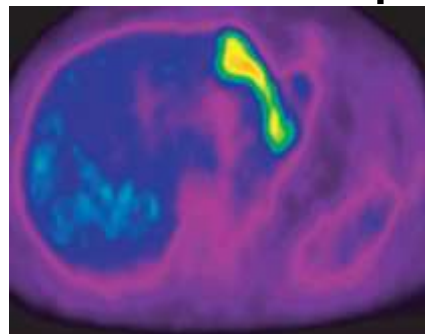
# The use of $^{18}\text{F}$ FDG-PET as a marker of tumor responsiveness to neoadjuvant treatment



- On CT, treatment response may be underestimated by treatment related changes such as fibrosis, necrosis, inflammation, and edema
- **FDG** ; early and sensitive pharmacodynamic marker of tumor response represents viable tumor cell number and a reduction reflect the tumor cell killing rate
- Good correlations between changes in FDG uptake & histopathological responses



At staging



status post 1th chemo

J Clin Oncol 2003;21:4604-4610  
Clin Cancer Res 2008;14:2012-2018  
J Gastric Cancer 2014;14(1):1-6

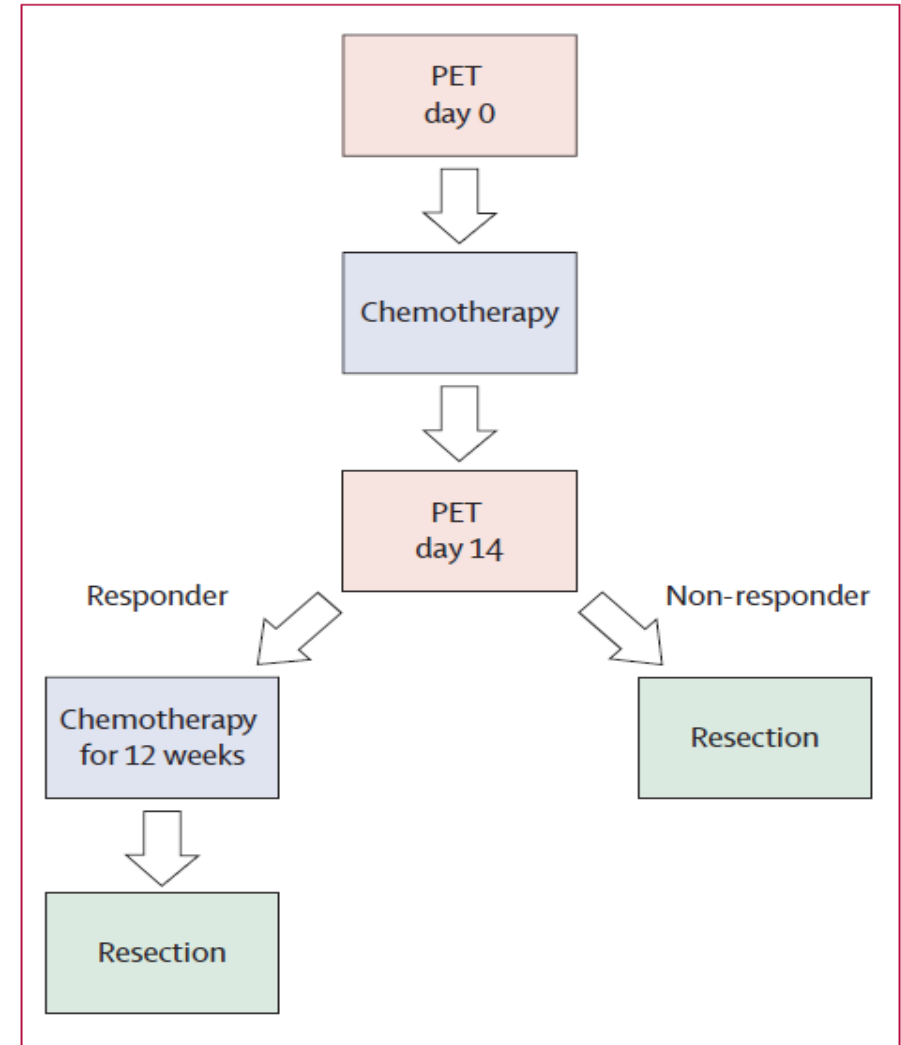


# The use of $^{18}\text{F}$ FDG-PET as a marker of tumor responsiveness to neoadjuvant treatment



## MUNICON phase II trial

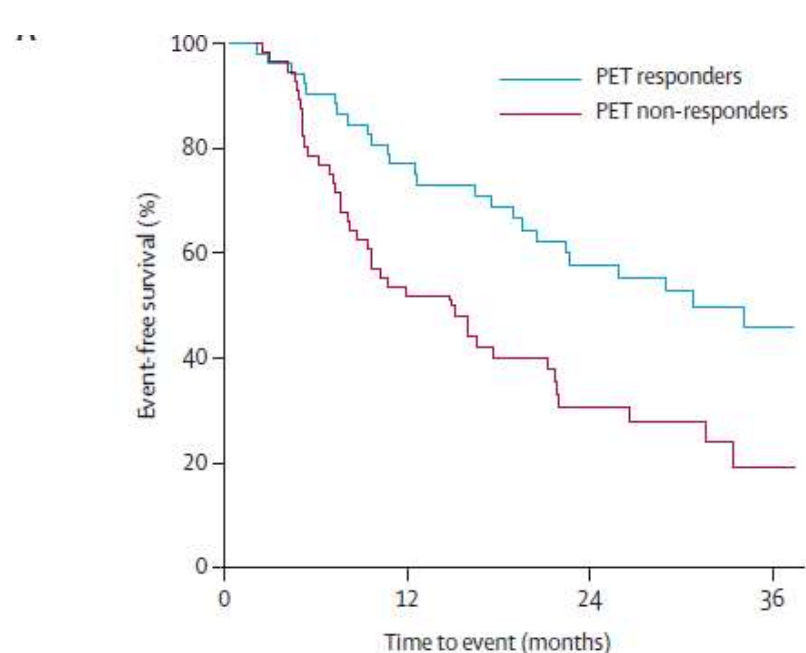
- 110 patients were evaluable for metabolic responses
- Decrease of 35% or more in tumour glucose SUV



# The use of $^{18}\text{F}$ FDG-PET as a marker of tumor responsiveness to neoadjuvant treatment



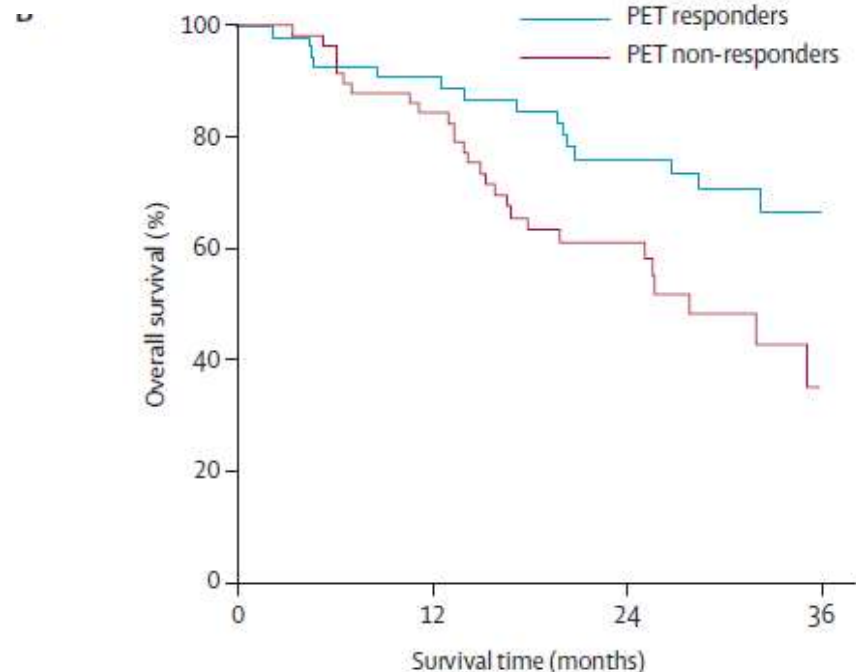
## MUNICON phase II trial



**Number at risk**

	0	12	24	36
PET responders*	54	38	24	11
PET non-responders†	56	29	13	2

**Event-free survival**



**Number at risk**

	0	12	24	36
PET responders*	54	46	30	13
PET non-responders†	56	45	21	4

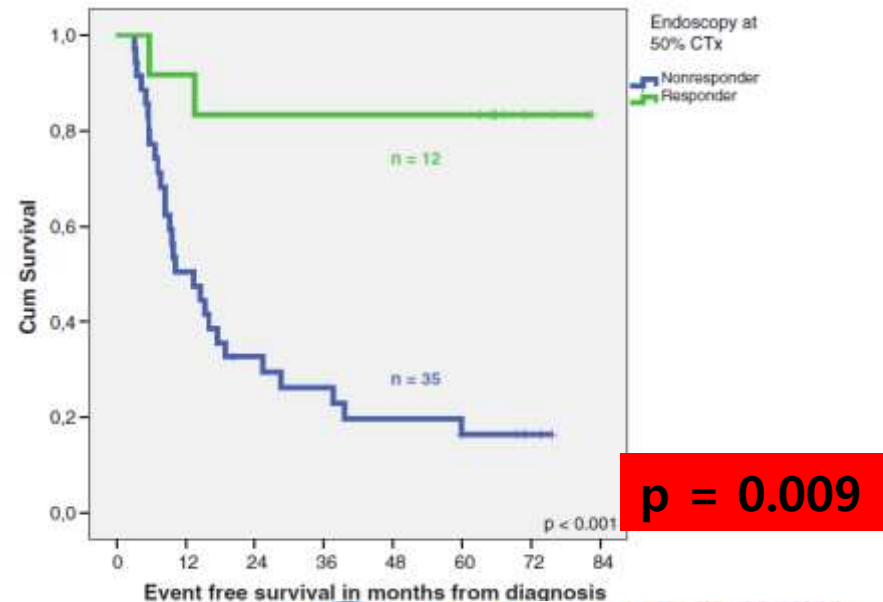
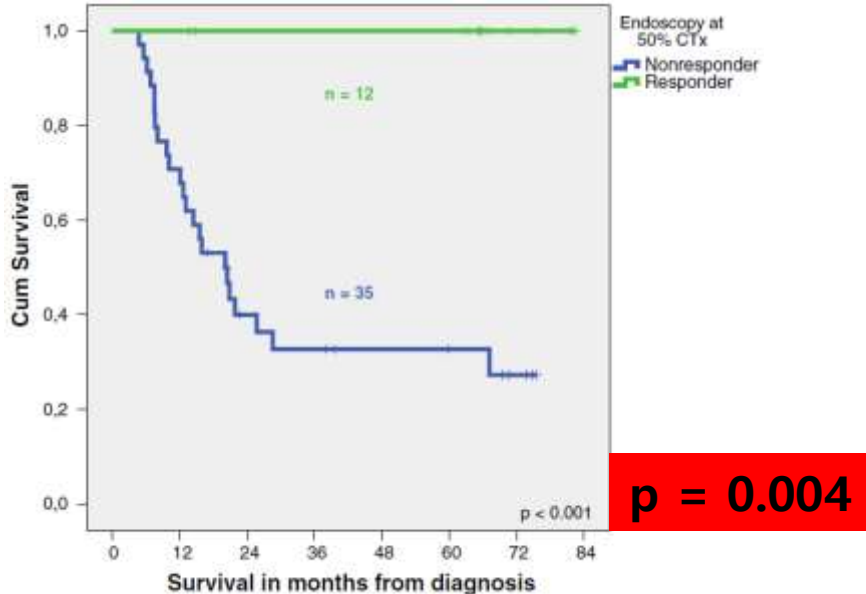
**Overall survival**

# Interim endoscopy results during neoadjuvant therapy for gastric cancer correlate with histopathological response and prognosis



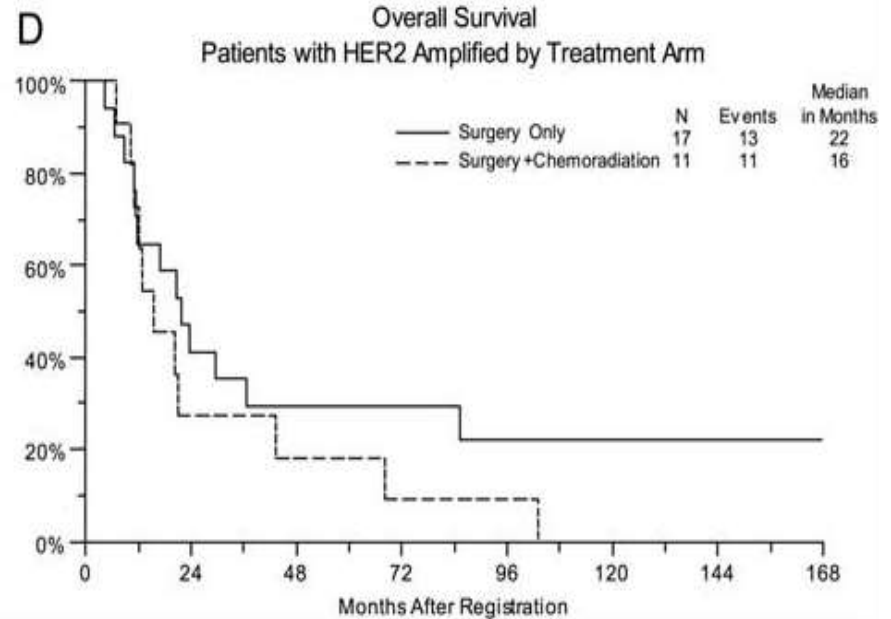
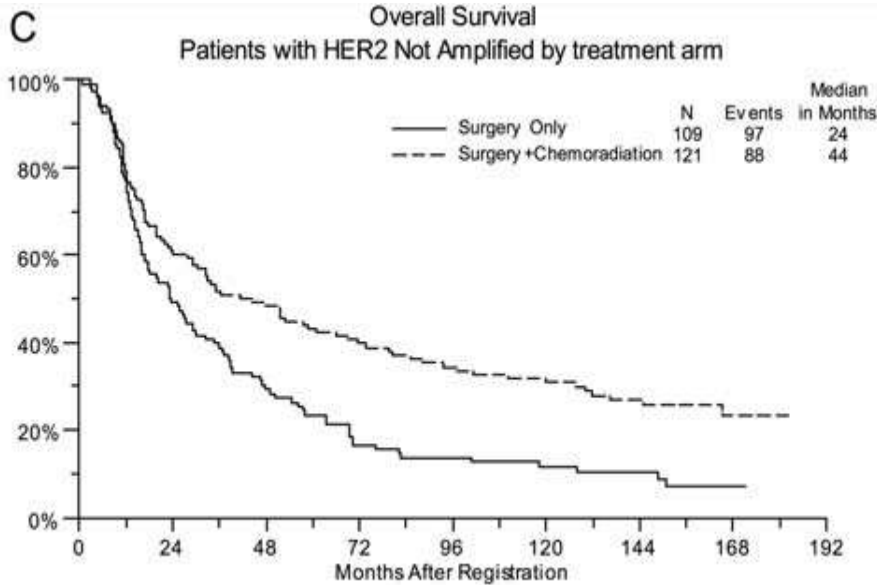
Interim endoscopic response was assessed after having received 50 % of the planned neoadjuvant chemotherapy.

Clinical response	Endoscopy	CT scan
CR = complete response	No residual tumor confirmation after 6 weeks	No residual tumor
PR = partial response	Decrease of intraluminal tumor >75 %	>50 % decrease of wall thickness
MR = minor response	Decrease of intraluminal tumor 75–25 %	50–25 % decrease of wall thickness
NC = no change	25 % decrease to 25 % increase of intraluminal tumor	25 % decrease to 25 % increase of wall thickness
PD = progressive disease	Increase >25 % of intraluminal tumor	Increase >25 % of wall thickness or distant metastases



# Assessment of *HER2* gene amplification in adenocarcinomas of the stomach or gastroesophageal junction in the INT-0116/SWOG9008 clinical trial

M. A. Gordon<sup>1</sup>, H. M. Gundacker<sup>2</sup>, J. Benedetti<sup>2</sup>, J. S. Macdonald<sup>3</sup>, J. C. Baranda<sup>4</sup>, W. J. Levin<sup>5</sup>, C. D. Blanke<sup>7</sup>, W. Elatre<sup>1</sup>, P. Weng<sup>1</sup>, J. Y. Zhou<sup>1</sup>, H. J. Lenz<sup>8</sup> & M. F. Press<sup>1\*</sup>



- *HER2* served as a predictive marker of response to therapy, not a prognostic marker
- Cancer cells overexpressing *HER2* show radiation resistance compared with cancer cells lacking *HER2*

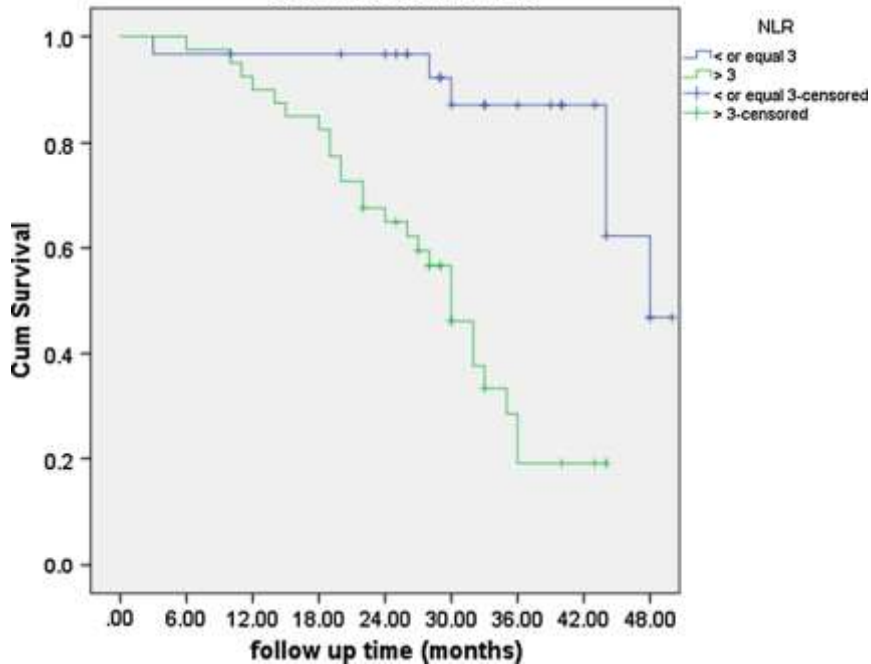


# Blood neutrophil-lymphocyte ratio predicts survival in locally advanced cancer stomach treated with neoadjuvant chemotherapy FOLFOX 4

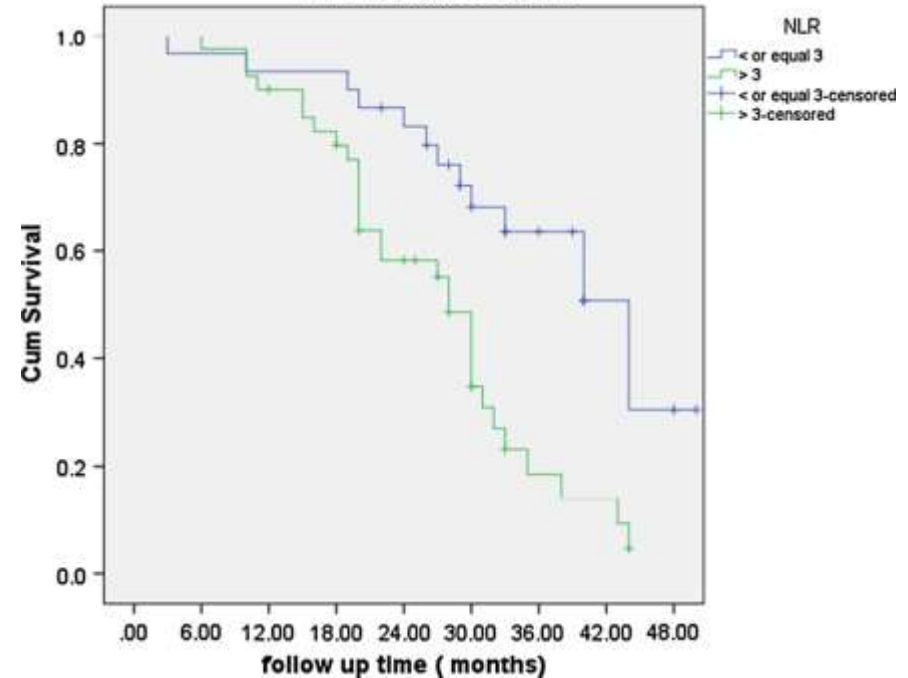


NLR was divided into two groups: high ( $> 3$ ) and low ( $< 3$ ).

OAS in relation to NLR



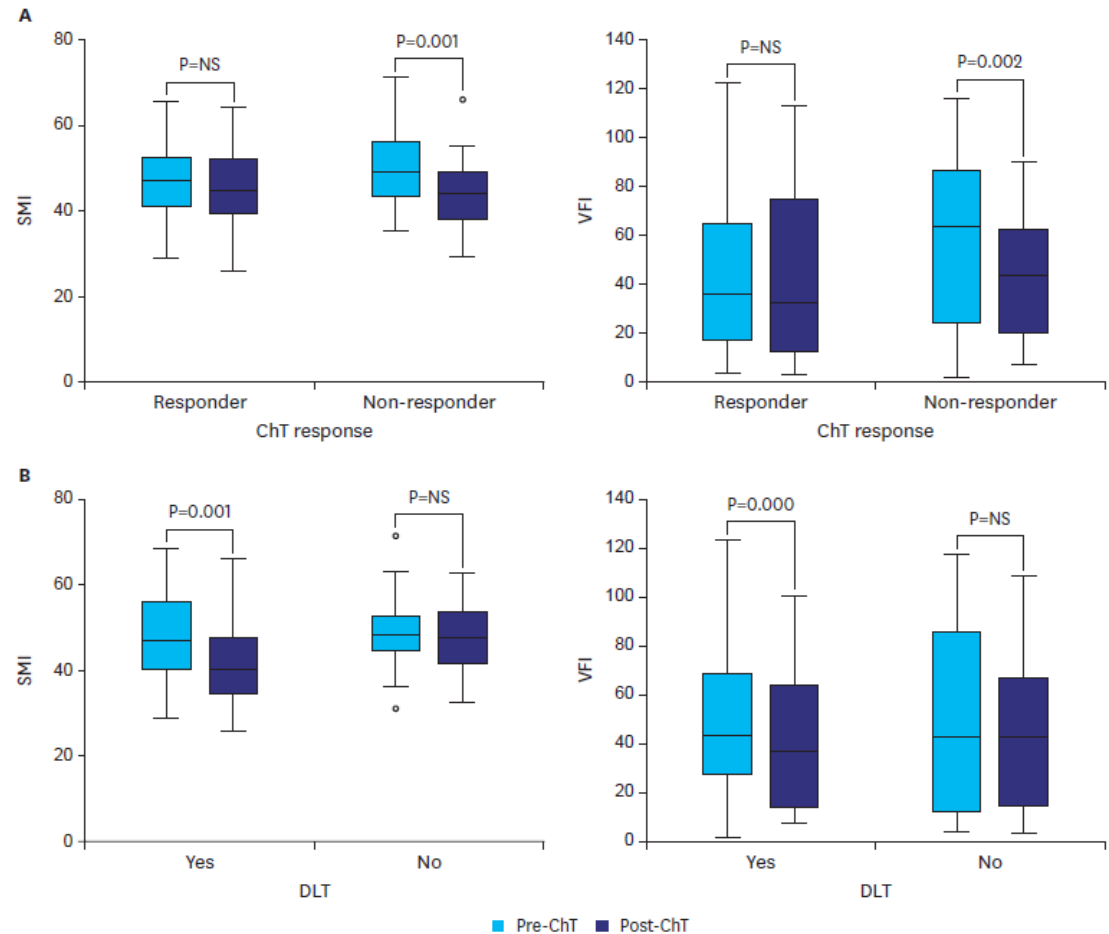
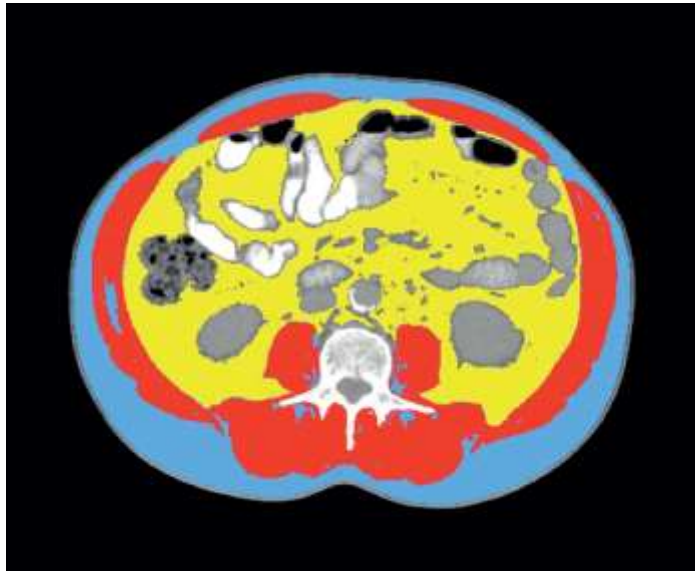
PFS in relation to NLR



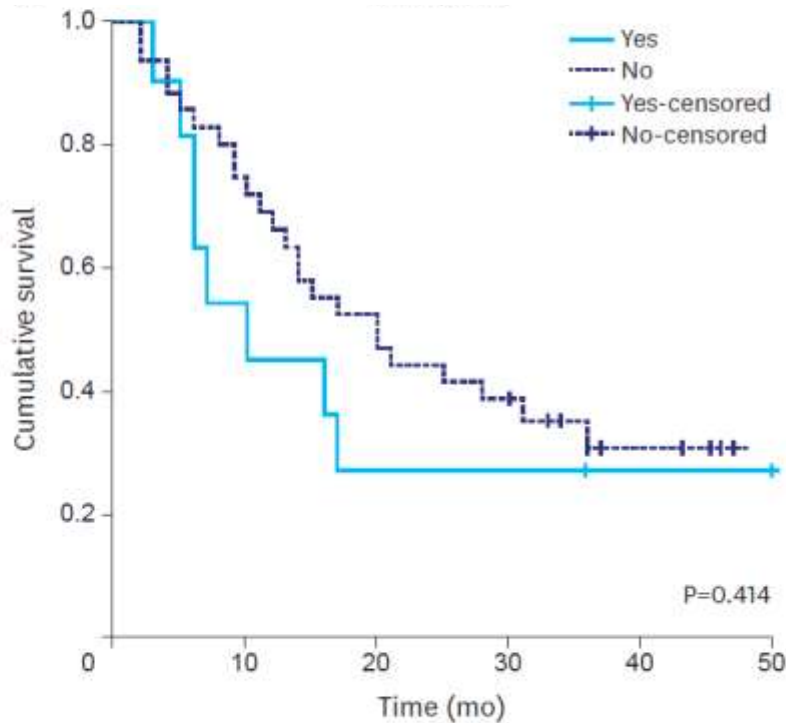
Overall survival in relation to NLR

Progression-free survival in relation to NLR

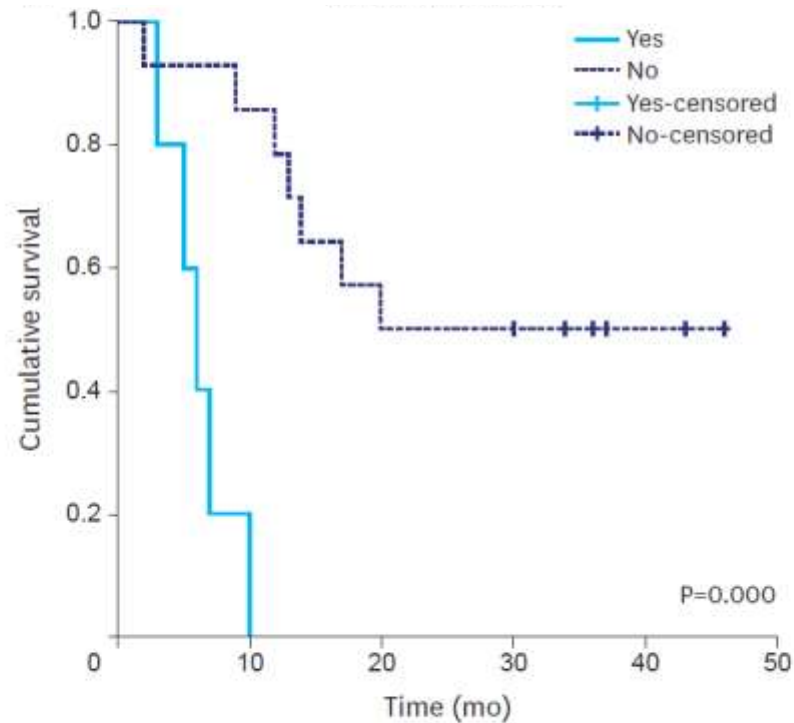
# Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer



# Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer



**Sarcopenia**



**Sarcopenia obesity**

# Summary



- Evidences supporting benefit of neoadjuvant therapy in locally advanced gastric cancer are **not sufficient, especially in Korea.**
- **Selected patients with marginally/potentially resectable disease** may be a candidate of neoadjuvant therapy, benefit of which also should be verified in the ongoing study.
- In the treatment of Locally-advanced, marginally resectable gastric cancer, individualized treatment & **multidisciplinary assessment** is necessary



# Future directions



- The exact role of neoadjuvant chemotherapy in patients treated with D2 dissection will be proven in the **ongoing phase III clinical trial**
- 5-fluorouracil-based combination chemo regimen is limited, increasing recognition of the potential benefit of **therapies of targeting molecular** characteristics such as HER2, VEGF and **immunotherapy**(PD-1 & PDL-1) into the perioperative setting

**Thank you  
for your attention**

