

HAVE WE MADE ANY PROGRESS IN THE TREATMENT OF ADVANCED GASTRIC CANCER?

ESMO CONFERENCE: 11TH WORLD CONGRESS ON GASTROINTESTINAL CANCER

SESSION VII: GASTRIC CANCER

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Current Questions in Advanced Gastric Cancer Management

- Which are the aims of therapy?
- Should patients with advanced gastric cancer receive chemotherapy and when?
- Which are the main prognostic factors?
- Is primary tumor location relevant for treatment decisions?
- Which are the active drugs?
- Is there any standard combination of drugs?
- Why haven't we been successful in getting better treatment for this disease?

Which are the aims of therapy?

- Symptomatic control
- Improve QoL or avoid its deterioration
- Delay tumor progression
- Prolong survival

Should patients with advanced gastric cancer receive chemotherapy?

Study	Chemotherapy	BSC	Hazard Ratio (fixed)	95% CI
Murad 1993 ¹	30	10	0.33	0.17 to 0.64
Pyhonen 1995 ²	31	30	0.25	0.13 to 0.47
Schellhaas 1996 ³	52	51	0.48	0.33 to 0.74
Total (95% CI)	113	91	0.38	0.28 to 0.52

Test for heterogeneity: $\chi^2 = 3.32$ ($P = .18$)
Test for overall effect: $Z = 8.13$ ($P < .0001$)

Wagner A, et al. JCO 2006.

When should patients with advanced gastric cancer receive chemotherapy?

	INITIAL ELF-FULV	DELAYED CT AT PD
CT	100%	50%
TIME TO CT	8 DAYS	82 DAYS
QOL IMPROVEMENT	70%	25%
SURVIVAL	10 MONTHS	4 MONTHS

Glimelius B, et al. Ann Oncol 1994.

Is primary tumor location relevant for treatment decisions?

	Oesophagus	OGJ	Gastric
Median survival:	9.5 months	9.3 months	8.7 months
1-year survival:	36.8%	37.9%	36.1%
2-year survival:	12.4%	14.3%	13.1%

Log rank p = 0.677

Figure 3. Overall survival according to primary tumour origins.

Chau I, et al. Ann Oncol 2009.

What are the main prognostic factors?

PS 2
Liver mets
Peritoneal mets
↑Alkaline Phosphatase

Chau I, et al. J Clin Oncol 2004.

What are the main prognostic factors?

Group	Score	median OS	1-year Surv
Good	0	11.8 m	48.5%
Moderate	1 o 2	7.4 m	25.7%
Poor	3 o 4	4.1 m	11.0%

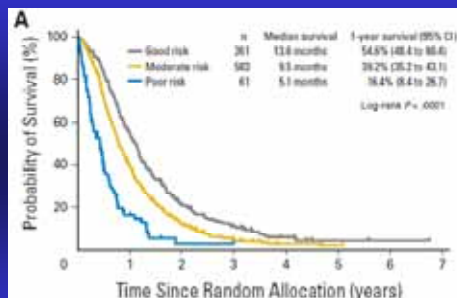
Chau I, et al. J Clin Oncol 2004.

What are the main prognostic factors?

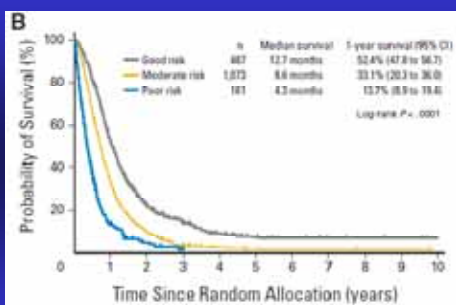
Table 1. Multivariate Baseline Prognostic Model for REAL-2 Study Patients

Factor	Hazard Ratio	95% CI	P
Performance status			
0-1	1		
2	2.044	1.533 to 2.725	<.0001
Liver metastasis	1.473	1.219 to 1.779	<.0001
Peritoneal metastasis	1.546	1.212 to 1.971	<.0001
Alkaline phosphatase ≥ 100 U/L	1.114	0.923 to 1.345	.14

Chau I, et al. J Clin Oncol 2009.



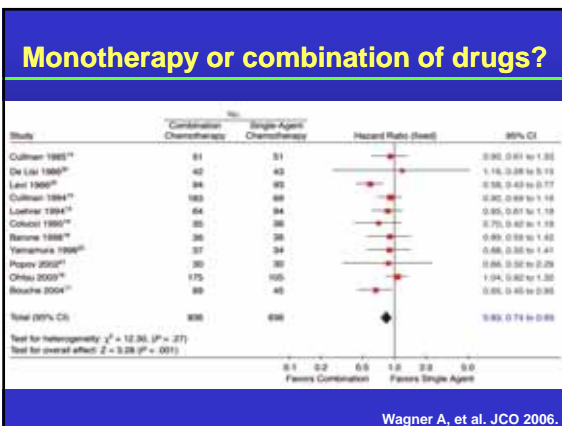
Chau I, et al. J Clin Oncol 2009.



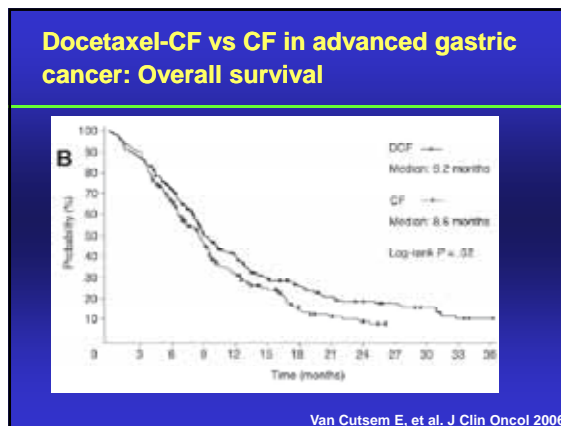
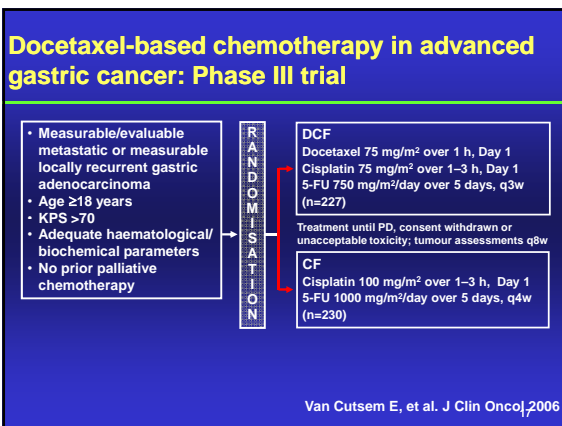
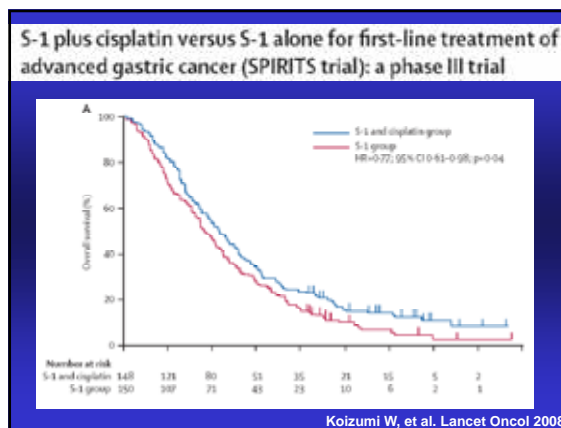
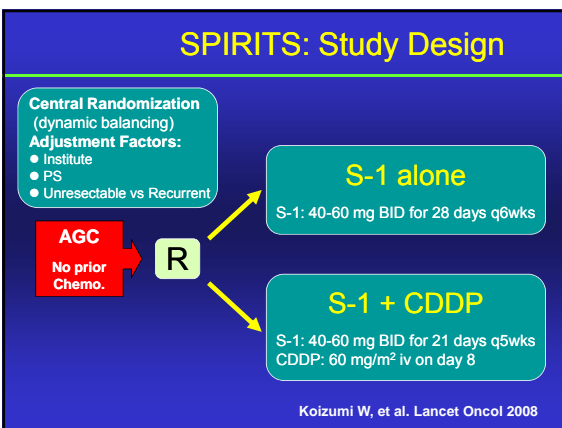
Chau I, et al. J Clin Oncol 2009.

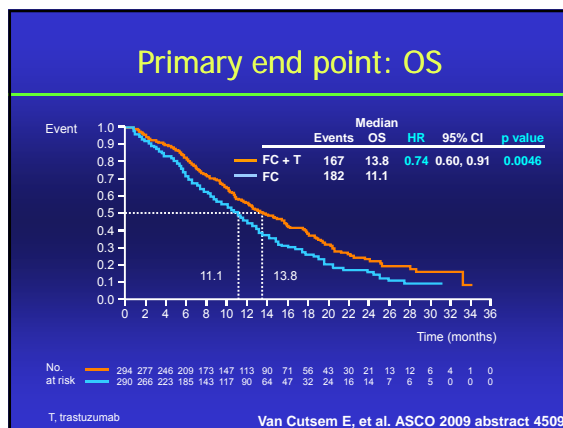
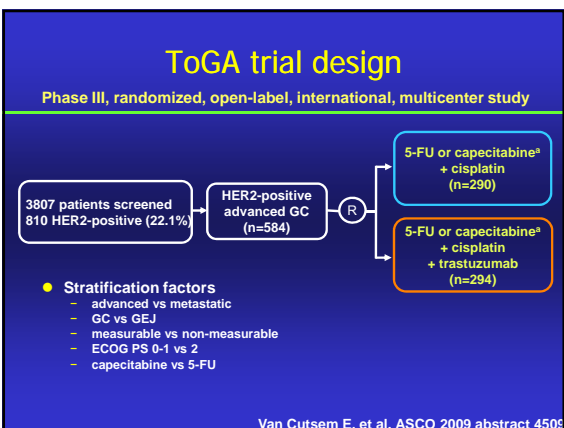
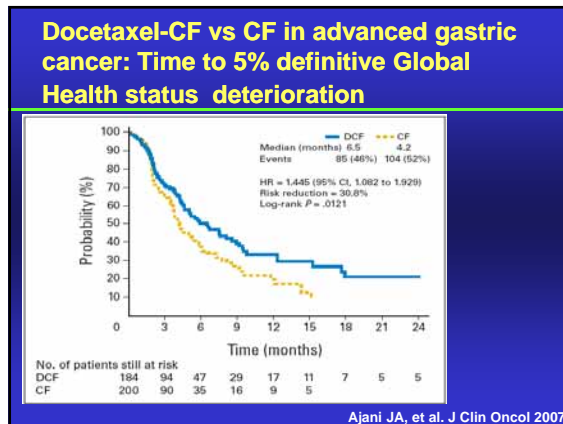
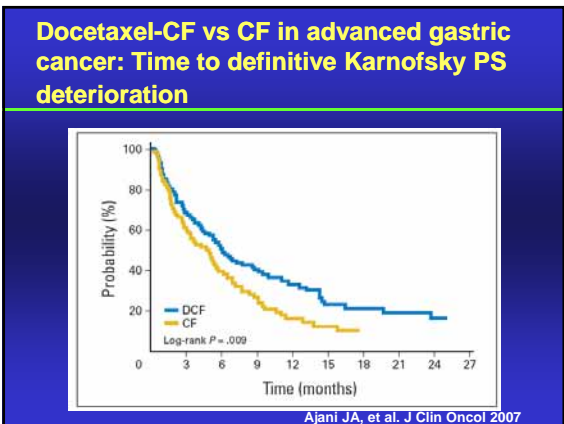
Which are the active drugs?

- 5-Fluorouracil
- Oral Fluoropyrimidines (capecitabine, S1, UFT)
- Anthracyclines?
- Cisplatin
- Oxaliplatin
- Docetaxel
- CPT-11
- Trastuzumab

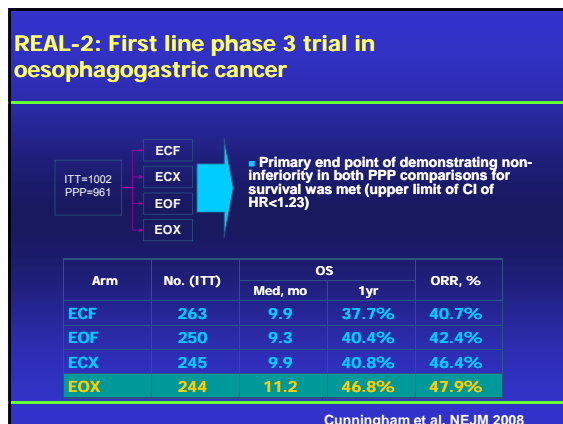


- ### What are the active drugs that have shown superiority in randomized trials?
- 5-Fluorouracil
 - Oral Fluoropyrimidines (capecitabine, S1, UFT)
 - Anthracyclines?
 - Cisplatin
 - Oxaliplatin
 - Docetaxel
 - CPT-11
 - Transtuzumab

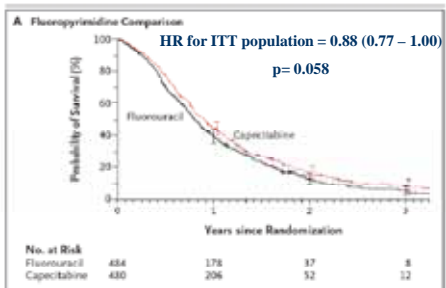




- ### What are the active drugs that have shown non inferiority in randomized trials?
- 5-Fluorouracil
 - Oral Fluoropyrimidines (Capecitabine, S1, UFT)
 - Anthracyclines?
 - Cisplatin
 - Oxaliplatin
 - Docetaxel
 - CPT-11
 - Transtuzumab

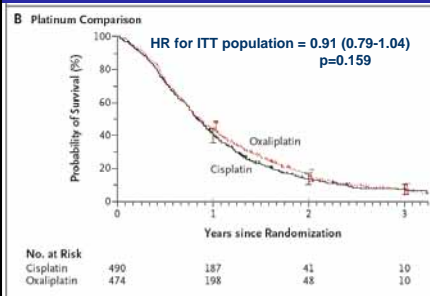


REAL-2: Overall survival fluoropyrimidin comparison



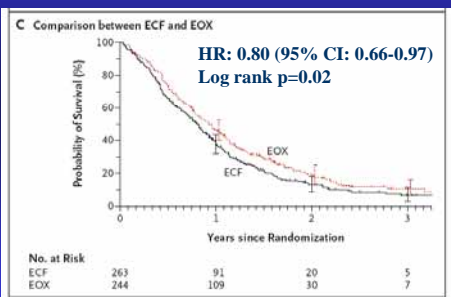
Cunningham et al, NEJM 2008

REAL-2: Overall survival platinum comparison



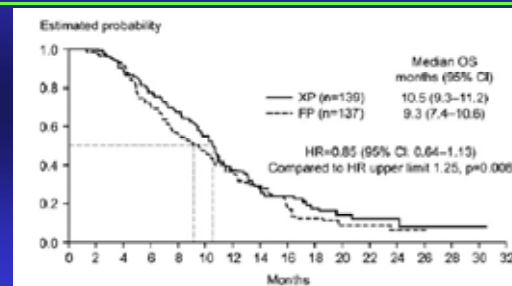
Cunningham et al, NEJM 2008

REAL-2: Overall survival: ECF vs EOX comparison



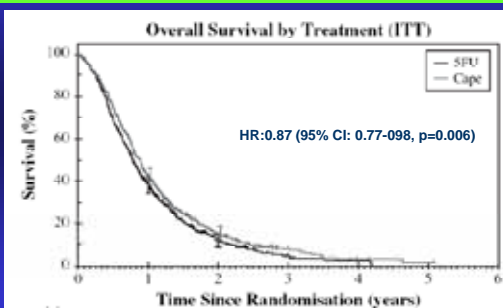
Cunningham et al, NEJM 2008

5-FU CDDP VERSUS CAPECITABINE-CDDP. A RANDOMISED PHASE III NONINFERIORITY TRIAL (ML17032)



Kang YK et al, Ann Oncol 2009

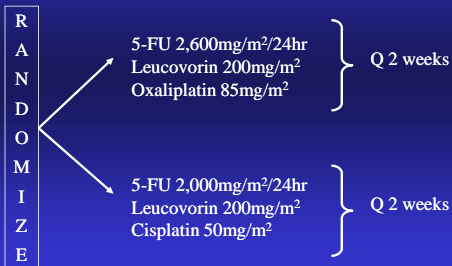
5-FU VERSUS CAPECITABINE A META-ANALYSIS OF REAL2 AND ML17032



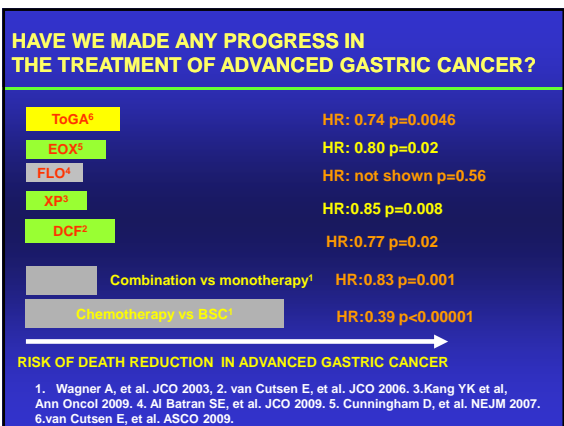
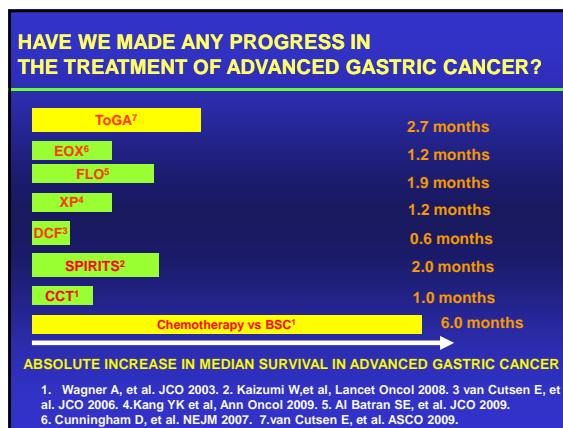
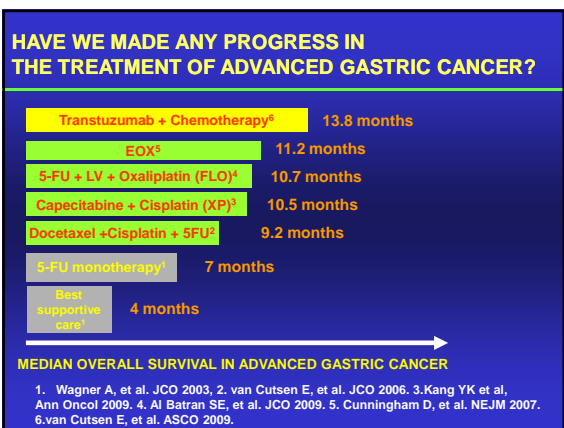
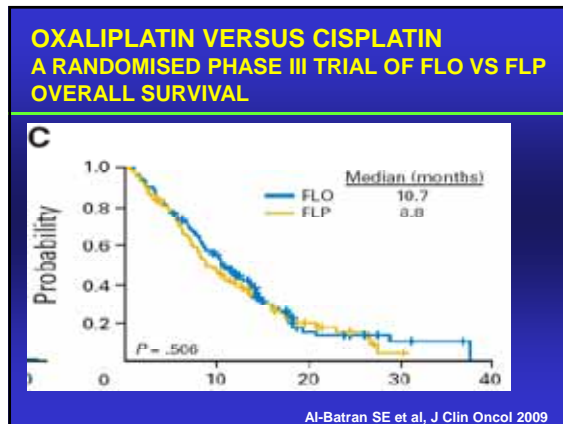
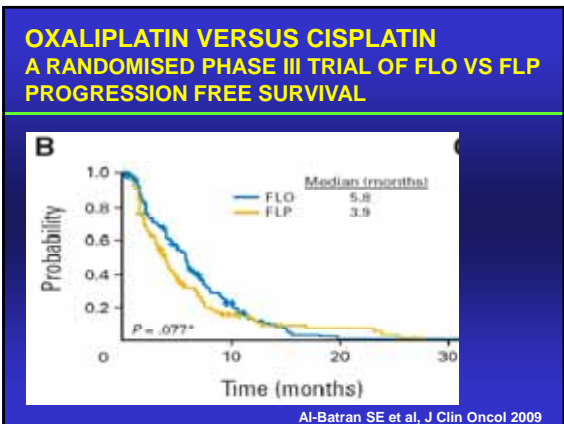
Okines AFC et al, Ann Oncol 2009

5-FU, LV, Oxaliplatin (FLO) vs. 5-FU, LV, Cisplatin (FLP) in Advanced Gastroesophageal Adenocarcinoma

220 patients with advanced gastric cancer:



Al-Batran SE et al, J Clin Oncol 2009



- ### Recommended approach to advanced gastric cancer patients
- Select patients with PS0-1 to participate in clinical trials
 - CT should have a palliative role
 - Patient reported outcomes of value
 - Assess the risk of toxicity vs benefit
 - TCF, ECF, EOX, XP or similar schedules of value
 - Consider second line therapy for selected patients. More trials on this point are needed

Recommended approach to improve results on gastric cancer patients

- Design better clinical trials within academic and community centers
- International Cooperation
- Biological agents should be studied in randomized trials
- Further studies on better predictive and prognostic biomarkers

Thank you

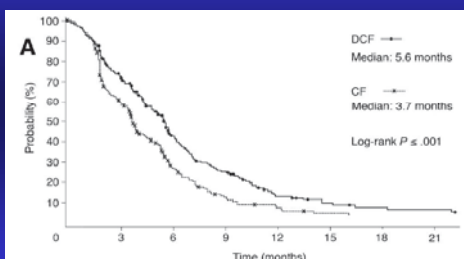
Back up

5-FU VERSUS CAPECITABINE A META-ANALYSIS OF REAL2 AND ML17032

Variable	Group	No. of patients (n)	Hazard ratio for OS (95% CI)	Significance
Performance status	0-1	1175	1.87 (1.55-2.26)	P = 0.000
	2	138		
Age	<60 years	582	0.83 (0.73-0.94)	P = 0.0026
	≥60 years	731		
Extent of disease	Locally advanced disease	273	1.64 (1.40-1.91)	P = 0.000
	Metastatic disease	1040		
Treatment	5-FU based	660	0.87 (0.77-0.98)	P = 0.0209
	Capecitabine based	653		
Histopathological subtype	Adenocarcinoma	1216		No significant effect
	Squamous cell carcinoma	97		

Okines AFC et al, Ann Oncol 2009

Docetaxel-CF vs CF in advanced gastric cancer: Progression free survival



Van Cutsem E, et al. J Clin Oncol 2006