CANCER OF ESOPHAGUS

I Sturm et al (JCO 2001;19:2272-81). N=53, all resected esophageal cancer. MOS 13.7 mo. Increase BNAX had better MOS 19.5 mo vs 8 mo; increase p16 also better survival MOS 23.8 vs 9.7 mo. Best results when both were high (MOS 45.8 mo).

K Schumacher et al (Ca Res 2001;61:3932-6). CD8+ cells present in 9/25 stage I-II and in 2/45 advanced stage III-IV. Multivariate analysis indicate HR 0.5 for survival when T8 cells were present.

M Tachibana et al (Cancer 2002;94:1955-60). PTEN expression is a favorable factor for OS.

W Ye et al (JNCI 2004;96:388-96). HP infection (decreased acid secretion and gastric atrophy) relates to lower incidence of esophagus adenocarcinoma (HR=0.3). Contrary results with CagA strain which increase esophageal squamous cell carcinoma (HR=2.1).

J Izzo et al (JCO 2006;24:748-54). N=43. NFKb expression associated with vascular and lymph vessel invasion. 8/21 NFKB+ developed metastasis and 0/22 NFKB- developed metastasis.

KL Wang et al (Clin Ca Res 2006;12:4598-604). Annexin A1 expression present ion 39% adenocarcinoma of gastroesophageal junction (41/104) and correlate with advanced stage, high recurrence rate and low OS (Median 12 mo vs 24 mo).


S Lagarde et al (JCO 2006;24:4347-55). Prognostic factors in adenocarcinoma of esophagus/gastroesophageal junction: Clinical factors: operation, Complication rates, Age, Sex, Tumor location and Barretts mucosa had all minor impact. Pathological factors: TNM staging very large impact. Others including grade, location of lymph noces, vessel invasion and response to therapy had minor impact.


CANCER OF ESOPHAGUS- BARRETT’S ESOPHAGUS

L Gossner (Cancer 1999;86:1921-8). 5 aminolevulinic acid (60 mg/kg) → 24 h later laser dye system irradiation with wavelengt 635 mm at a light dose of 150 J/cm2. Dysplasia length range 0.5-9 cm (mean 2.5 cm), all cured. High grade dysplasia median Fup 16.9 mo, cured in all patients. In superficial cancer 10/19 tumors had resolved with a mean of 1.7 sessions. No morbidity.

K Bani-Hani et al (JNCI 2000:92:1316-21). Cyclin D1 expression increase the risk of adenocarcinomin ain Barretts esophagus OR=6.85. N=307, Mfup 3.5y; 12 adenocarcinoma and 11/12 were Cyclin D1+. Other past findings including p53 and p16 were not so strong factors as Cyclin D1.

SJ Spechler et al (NEJM 2002;346:836). Review Barretts: High grade dysplasia leads to 5y esophageal cancer rate of 59%, requiring intense surveillance, endoscopic ablative therapy and esophagectomy. Progression of low grade dysplasia to high grade dysplasia in 10-28% in 5 y,
requiring endoscopy every 6-12 mo initially and then yearly (q 3-5 y in patients without dysplasia).

C Morales et al 8Lancet 2002;360:1587-9). Carcinogenetic events in Barretts: Squamous epithelium injured by reflux esophagitis → chronic inflammation condition plus genetic changes → Barretts metaplasia shows increased Cyclin D1, increased TGFα, p16 LOH/methylation, increase COX2 → low grade dysplasia appears and p53 mut or p53 LOH → high grade dysplasia with activated telomerase, and decrease E cadherin/catenin.

R Bresalier et al (Sem Oncol 2005;32:21-4). Barretts esophagus cancer incidence is 0.5%/year. Recommended endoscopic control q 3-5 y. Screening goal is to reduce 50% cancer incidence. The recommendations of the American Association is to screen all >50 yo with 5-10 year history of heartburn. In case of no dysplasia repeat q 3-5 y; low grade dysplasia repeat q 6-12 mo; & high grade dysplasia proceed to esophagectomy or endoscopic ablative therapies.

R Soetikno et al (JCO 2005;23:4490-8). Endoscopic resection of early Barretts and gastric cancer is very common in Japan. Indicated in well and moderately differentiated squamous cell carcinoma of the esophagus not invading lamina propria and without venous or lymphatic vessel involvement, avoiding circumferential lesions, and in well differentiated adenocarcinoma or papillary carcinoma confined to the mucosa, <2cm, not ulcerated, without venous or lymph vessel invasion. Techniques: Inject and cut; inject, lift and cut; cap technique (suction); ligation technique. CR 97% Barretts with a 10y recurrence rate of 10%. In gastric cancer DFS 99%, local recurrence 2-35%.

J Izzo et al (Sem Oncol 2007;34:2-6). Chronic gastroesophageal reflux leads to Barretts 0.5% annual transformation through the pathways of increased inflammatory cytokines, increased Cyclin D1 expression, and activation of NFκb. Low grade dysplasia associate to LOH 3p and 9p, and inactivation p16. High grade dysplasia associate to LOH or loss 4q, 8p, 13q, 14q and 17p, p53 mut, 20q and 8 q amplification, DNA aneuploidy and CpG methylation. Cancer associate to LOH or loss in 6p, 8q, 13p and 18 q.

**CANCER OF ESOPHAGUS-LOCOREGIONAL DI SEASE**

B Minsky et al (JCO 2002;20:1167-74). N=236, T1-4, N0-1, M F up 16.4 mo. Randomized to 5FU+CDDP + RT 64.8 Gy (MST 13.1 mo, 2 yOS 31%, Regional failures 56%) vs Same ChX + RT 50.4 Gy (MST 18.1 mo, 2 yOS 40%, Regional failures 52%). No improvement.

J Hulscher et al (NEJM 2002;347:1662-9). N=220., adenocarcinoma of distal esophagus/cardias, MFUp 4.7y. Randomized to transhiatal esophagectomy + lymphadenectomy (Postop complications 27%, 5 yOS 27%) vs Transtoracic esophagectomy + lymphadenectomy en block & extended (Postop complications 57%, 5 yOS 39%).

RC Esophageal cancer Working Group (Lancet 2002;359:1727-33). N=802. Randomized study to CDDP 80 mg/m2 + 5FU 1g/m2 qd x 4 x 2 cycles → surgery (Complete resection 60%, OS = .79, MST 16.8 mo, 2yOS 43%, 3yOS 29%) vs surgery alone (Complete resection 54%, OS = .79, MST 13.3 mo, 2yOS 34%, 3yOS 18%). Results better without adverse side effects for preop Chx. Both groups had optional preop RT and only 9% in each group had it.

P Bidoli et al (Cancer 2002;94:352-61). CDDP+5FU x 4 d x 2 + RT 30 Gy in 15F/19d → surgery (32/106 resected, 8 pCR, micro residuum 12, mortality 22%, PFS 24%, MST 12 mo, OS 9%) vs same + 2 additional chemotherapy + RT 20 Gy in 10 F (PFS 22%, MST 22 mo, OS 17%).

A Berger et al (J CO 2005;23:4330-7). Neoadjuvant chemo-radiotherapy (5Fu-CDDP-46Gy): CR correlated with survival (MOS 33 mo, 5yOS 26%). Difficult to assess the CR status without
surgery because EUS is not valid and PET not sensitive enough...

D Cunningham et al (NEJM 2006;355:11-20). N=319 evaluable deaths, Mfup 4y, adenocarcinoma of lower esophagus. Randomized study to EPI 50 mg/m2 d1+ CDDP 60 mg/m2 d1+ 5FU 200 mg/m2 civi x 21d x 3 cycles→ surgery→ 3 additional cycles (post op complications 46%, 5yOS 36%) vs surgery alone (postop complications 45%, 5yOS 23%), HRdeath=0.75 and HR5yPFS=0.66. Preop ChX conferred better OS.

L Bedenne et al (JCO 2007;25:1160-8). N=444, 88.8% squamous, T3 N0-1 M0. Randomized to CDDP+5FU d 1-5 & d22-26 x 3 cycles + RT 46Gy/4.5 wk or split 15 Gy d 1-5 & d22-26 (2yOS 40%, MST 19.3 mo, 3mo mortality 0.8%) vs surgery alone (2yOS 34%, MST 17.7 mo, 3mo mortality 9.3%). No need of surgery when there is an OR to ChX-RT!!.

G Crehange et al (JCO 2007;25:4895-901). Phase III randomized protracted vs split RT, Mfup 47.4 mo. RT 46 Gy/4.5 wk +/- 20 Gy +/- CDDP-5FU x 2 (N=161, OR 67%, 2yLRFS 76.7%, 2 yOS 37.1%) vs RT 1 wk 15 Gy x 2 +/- 1 wk 15 Gy +/- CDDP-5FU x 2 (N=285, OR 68%, 2yLRFS 56.8%, 2 yOS 30.5%), indicating better protracted RT.

J Tepper et al (JCO 2008;26:1086-92). N=475 planned, poor accrual, CALGB trial, closed with 56 pts and Mfup 6 y. Randomized to esophagectomy + ly no dissection (N=26, MST 1.79 y, 5 yOS 16%) vs CDDP+5FU + RT 50.4 Gy + Esophagectomy + ly no dissection (N=30, MST 4.48 y, 5yOS 39%). Satndard arm multimodality.

CANCER OF ESOPHAGUS-ADVANCED CHEMOTHERAPY

J Ajani et al (JCO 2006;24:663-7). N=47, median age 56yo, median KPS 80%. Treated with CDDP 75 mg/m2 d 1 + S1 po 25 mg/m2 bid d 1-21; repeat q 4 wk. OR 51%, 6mo alive 71%, MST 10.9 mo. Activity similar to CDDP+5FU.


D Cunningham et al (NEJM 2008;358:36-46). N=1002. Randomized to EPI+CDDP+5FU, EPI+CDDP+XEL, EPI+LOHP+5FU or EPI+LOHP+Xel nad found MST 9.9, 9.9, 9.3, and 11.2 mo respectively. HR=0.86 death for Xel vs 5FU; and HR=0.92 death for LOHP vs CDDP. NO significant differences. 1yOS were 37.7%, 40.8%, 40.4% and 46.8% respectively.

CANCER OF STOMACH

CANCER OF STOMACH- CARCINOGENESIS

H Brenner et al (cancer 2000; 88:274-9). H Pylori (CagA+ strain) and family history (Polymorphism IL1B 31T -E. El Omar, Nature 2000;404:398-402) were strong predictive factors of gastric cancer OR=8.2

MM Heiss et al (JCO 2002;20:2005-16). UPAR and PAI-1 in primary tumor correlated with the presence in metastases and bear a correlation with DFS/OS (RR=2.89, RR=1.72). Presence of cells in BM without UPAR/PAI-1 do not have prognostic significance.

C Figueiredo et al (JNCI 2002;94:1680-7). N=221 gastritis & N=222 gastric cancer. HP strains vacAs1, vacAm1, CagA+ increase risk of gastric cancer (OR=17). Polymorphism in IL1B (IL1B-S11T carriers) also had an increased risk (OR=3.3). Combinations of both factors gave OR=23.

WH Wang et al (JNCI 2003;95:1784-91). ASA and NSAID metanalysis of randomized studies indicated a reduction in gastric cancer incidencie in a dose related manner (OR=0.72). Prevention?

J Van Beek et al (JCO 2004;22:664-70). EBV associated gastric cancer (EBER \( \frac{1}{2} \) RNA in situ hybridization) present in 7.2% gastric cancers. Associated to a better prognosis, younger patients, male predominant, less lymph node metastases.

WK Leung et al (Clin Ca Res 2006;12:3216-21). H Pylori is a gastric carcinogen, mechanism is related to cagA+ strains, which associate to inflammation (IL1B, TNFa, IL10). E-cadherin methylation also relates to nuclear activation of transcription factors due to unopposed activity of B-catenin. Inherited E-cadherin mutations lead to HDGC. Normal mucosa ( after HP infection) \( \rightarrow \) superficial gastritis & intestinal metaplasia (cagA island related TNFa, IL10, IL1; or Ecadherin hypermethylation) \( \rightarrow \) dysplasia \( \rightarrow \) gastric adenocarcinoma.

SK Shin et al (Cancer 2006;107:481-8). JC virus (polyoma virus) present in GI tract is a T-Ag responsible of carcinogenesis. Studied DNA from 23 gastric cancers and found T-Ag, JCV and VP-1 (capsid gene) in 567%, 57% and 30% of the cases respectively...

M de Maat et al (JCO 2007;25:4887-94). N=40. Methylation of COX2 detected in 23-28% of samples. HR=0.49 for TTP and HR=0.62 for OS. COX2 silencing carried a better prognosis.

M Higashiyama et al (Ann Surg Oncol 2007;14:3419-22). N=295 with immunohistochemistry of osteopontin positive in 205/295. N=18 studied with osteopontin mRNA, and found it was present in 15/18 (83%). High level expression correlated with poor prognosis, mets, high grade and tumor depth. Prediction of metastases: MOS osteopontin negative >100 mo, osteopontin ++ MOS 60 mo; & osteopontin +++ MOS 30 mo.

**CANCER OF STOMACH- HEREDITARY GASTRIC CANCER**

W Grady et al (Nature Gen 2000;26:16-18). Hereditary diffuse gastric cancer (HDGC) is associated to E-cadherin mutation (CDH-1 gene). The second allele do not have LOH but in a half of the cases the promoter is methylated in the second allele (second hit model).


R M Cisco et al (Cancer 2008;113:1850-6). HDGC is an autosomal-dominant inherited cancer syndrome with inactivating mutation of E-Cadherin gene CDH1, identified in 30-50% family risk individuals (10% incidence). Carriers have a 70% lifetime risk of gastric cancer. Women also 20-40% risk of lobular breast cancer. Recommendation is total gastrectomy at least 5 y younger than the youngest relative (often microscopic HDGC found in resection samples).
CANCER OF STOMACH: LOCALIZED DISEASE

Gianni L (Ann Oncol 2000;11:62-3). Metanalysis of adjuvant chemotherapy trials HR=0.72


C Rossi et al (cancer 2002;94:492-9). Surgery + Hyperthermia (42.5°C mean ip temperature x 90 min) with ADM MTD 15.25 mg/L-1 + CDDP 43 mg/L-1 (in 4-5 L perfusate at a rate 500-1000 mL/min. Mfup 19 mo. DFS 35% (gastric carcinoma and sarcoma).


T Sano et al (JCO 2004;22:2767-73). Japan Clinical Oncology Group. N=523, T2-4. Randomized study to D2 lymphadenectomy (postop complication rate 20.9%) vs paraortic lymphadenectomy (extended) (postop complication rate 28.1%). Complications were: anatomic leak, pancreatic fistula, abdominal abscess and pneumonia. No differences in postop mortality 0.8% in each group.

M Armanios et al (JCO 2004;22:4495-99). T2-4 N+ adenocarcinoma odf esophagus, gastroesophageal junction and cardias. Adjuvant chemotherapy TXL 175 mg/m2 + CDDP 75 mg/m2 q 3 wk. N=59, 89% ly no +, R0 resections. Toxicity grade 3-4, 56%. M F up 4 y, 2 yOS 60%.

J A Ajani et al (JCO 2005;23:1237-44). N=41. Neoadjuvant ChX+RT. N=41, 83% proximal cancer. TXL + 5FU + CDDP → RT 45 Gy + TXL + 5FU → Surgery. Completed 98%: 78% R0 resection (5yOS 80%), pCR 20% (5yOS 100%) and pPR (<10% cancer cells) 15%.

D Cunningham et al (NEJM 2006;355:11-20). Randomized ECF pre/postop (N=250, 5yOS 36%), vs surgery (N=253, 5yOS 23%).

E Newman et al (Sem Oncol 2005;32:S97-S100). N=32, T3N0, T4N0, TN1 & TN2, M F up 28 mo. Preop Chx CPT 75 mg/m2 + CDDP 25 mg/m2/wk x 4 → 2 wk rest → surgery → ip chemotherapy Fluoruridine 3 g x 3 d + ip CDDP 60 mg/m2 d 3 x 2 cycles. NED 10 (31.3%), AWD 4 (12.5%), DWD 13 (40.6%), DNED 5 (15.6%), MOS 36.5 mo, R0 patients had no recurrences.

J A Ajani et al (JCO 2006;24:3953-8). Localized gastric cancer N=49, 20 institutions. CDDP+5FU-FA x 2 → TXL wkly + 5FU civi + EBR T → surgery at 5-6 wks. Results: pCR 26%, R0 resection 77%, 1 yOS pCR 82%, and 1yOS less than pCR 69%. Suggest Phase III comparing to postop ChX-RTX.

S Sakuramoto et al (NEJM 2007;357:1810-20). Stage II-III, D2 resection. Randomized to surgery + S1 adjuvant 80 mg/m2 qd cx 4 q 6 wk x 1 y (N=529, 3yOS 80.1%, HR death=0.68) vs surgery alone (N530, 3yOS 70.1%). Effective in East-Asian.

M Sasako et al Japan Clinical Oncology Group (NEJM 2008;359:453-62). Randomized to D2 lymphadenectomy (N=263, surgical complications 20.9%, 30d death rate 0.8%, 5 yOS 69.2%, HR death=1.03, HR recurrence=1.08), vs D2 + Paraortic nodal dissection (N=260, surgical complications 28.1%, 30d death rate 0.8%, 5 yOS 70.3%) NO improvement.

R Persiani et al (Ann Surg Oncol 2008). N=24, 7 y F up. EPI + VP + CDDP x 3 → D2 surgery (R0 resection 83.3%, no pT0, downstaging 41%) → EPI + VP + CDDP x 3. Achieved full therapy 71%. MOS 49 mo, 7yOS 40%.
FD Costanzo et al (JNCI 2008;100:388-98). N=258, surgery first, M F up 72 mo. Randomized to PELF x 4 (HR recurrence=0.92, HR survival=0.90) vs control. Found 10% reduction in relapse and death rate.

CANCER OF STOMACH-ADVANCED CHEMOTHERAPY

T Yamao et al (Ann Oncol 2001;12:1729-35). Escalation CPT dose. CPT 150 mg/m2 q 2 wk + Mitoc 5 mg/m2 q 2 wk. Adequate toxicity. Results: 15/31 PR (14 prior therapy); MDR 3 mo, 1 yOS 36%.

Y Jeen et al (Cancer 2001;91:2288-93). N=52. EPI 50 mg/m2 d 1 + CDDP 60 mg/m2 d 1 + UFT (Tegafur-Uracil) 360 mg/m2/qd po + FA 45 mg/d po x 21 d q 4 wk. Results: 3 CR + 24 PR (OR 57.5%). MOS 15 mo.

L Celio et al INT Milan (Sem Oncol 2002;29:63-8). Premetrexed 500 mg/m2 q 3 wk (+VitB12 + FA). N=30 evaluable. Results: 2 CR + 5 PR + 4 NC (OR 22%). MDR 4.4 mo.

A Reichle et al (BMT 2003;32:665-71). N=25, metsgastric cancer. EAP (DOX 40 mg/m2 x 2 + VP 120 mg/m2 x 2 + CDDP 40 mg/m2 x 2 + GCSF + apheresis + HDChX VP 500 mg?M2 x 3 + CDDP 50 mg/m2 x 3 + Mitoc 10 mg/m2 + BCNU 300 mg/M2 x 2 cycles + ASCT. OR 77%, 12-14 achieved R0 resection (8 prior carcinomatosis), Mfup 3.2 y, 4 patients alive. MOS 8.4 mo.

SE Al-Batran et al (JCO 2004;22:658-63). 5FU 2.6 g/m2 civi 24 h + FA 500 mg/m2 (2 h iv) + LOHP 85 mg/m2, q 2 wk. N=37. OR 43%, NC 32%, PD 24%. MOS 9.6 mo. Well tolerated.

O Bouche et al (JCO 2004;22:4319-28). N=136. Randomized to FA 200 mg/m2 2 h uiv → 5FU bolus 400 mg/m2 + 5FU 22 h civi 600 mg/m2 x 2 days (OR 13%, MPFS 3.2 mo, MOS 6.8 mo) vs LF5FU2 + CDDP 50 mg/m2 d 1 (OR 27%, MPFS 4.92 mo, MOS 9.5 mo); vs LV5FU2 + CPT 180 mg/m2 d 1 (OR 40%, MPFS 6.9 mo, MOS 11.3 mo) Quite promising.

J Ajani et al (JCO 2005;23:5660-7). N=158. TXT 75 mg/m2 + CDDP 75 mg/m2 q 3 wk (ORR 26%, MTTP 5 mo, MOS 10.5 mo) vs TXT + CDDP + 5FU 750 mg/m2/d civi x 5 (ORR 43%, MTTP 5.9 mo, MOS 9.6 mo). Now coparing with CDDP + 5FU alone.

J Ajani et al (JCO 2005;23:6957-65). CDDP 75 mg/m2 d 1 + S-1 1-21 (50 mg/m2/d x 21d, lower than Japan study with 80 mg/m2). Results: 6/16 PR. PK was different in Japan and Europe-USA with higher TF levels in Japan.

J Ajani (Cancer 2006;107-221-31). Medline Review of Xeloda in gastric, gastroesophageal and esophageal cancer. XEL is absorbed in the GI tract and converted in the liver to 5’DFCR and 5’DFUR (carboxylase and cytidine deaminase). 5FU series included Phase II-III iv, oral UFT and oral S-1. OR about 50% (in combination chemotherapy, maximal response rate). Xel series (Phase II-III) had OR 65% in combination chemotherapy with LOHP, CPT, TXT & TXL, maximal response rate). Current combinations include XEL with LOGHP, TXT and CPT.

A Wagner et al (JCO 2006;24:2903-9). Systematic review meta-analysis. 5fu+ADM> 5FU; 5FU + ADM + CDDP > 5FU + ADM (HR=0.83, best 3 drug schedule); CPT + 5FU > 5FU + other (ADM/CDDP) (HR=0.88, non significant). Now testing 5FU + CPT + third agent never tried before...

AJ Lenz et al (cancer 2007;109:33-40). S-1 (Tegafur –prodrug 5FU + 5-chloro 2,4 hydroxypyrimidine –prevents degradation SFU + Oxonate –avoids diarrhea from 5FU) MTD 25 mg/m2 bid d 1-21 in Western patients, with distinct CYP2A6. Combined therapy with CDDP 75 mg/m2 d 1 + S-1 25 mg/m2 bid d 1-21 q 4 wk (N=72, OR 55% + NC 30%; MST 10.4 mo, 2 yOS 21%; hematological toxicity gr 3-4 WBC 19%, Plat 1%, Hb 6%, fatigue 24%, N&V
XEL is a good substitute but not superior to 5FU. FLAG triasl compares S-1 + CDDP vs 5FU + CDDP.

T Dragovich et al (JCO 2006;24:4922-7) Phase II Tarceva in gastroesophageal (N=43) and gastric adenocarcinoma (N25). Rash 86%, fatigue 50%, liver enzymes 28%, OR: 1 CR + 4 PR, MST 6.7 mo 9% OR in GEC, NO EGFR mutations, inactive in gastric cancer.

M Shah et al (JCO 2006;24:5201-6). N=47, unresectable. BV 15 mg/kg d 1 + CPT 65 mg/m2 d 1 & 8 + CDDP 30 mg/m2 d 1 & 8 q 3 wk. Toxicity: 28% hypertension, 2 gastric perforation, 1 ulcer perforation, 1 myocardial infarction (4 severe toxicity), TEP 125%. M Fup 12 mo. MTTP 8.3 mo, OR 65%, MST 12.3 mo. Indicate reductyion of BV to 5 mg/kg... Mentioned toxicity...

E Van Cutsem et al (JCO 2006;24:4991-7). N=445. Randomized study: TXT 75 mg/m2 + CDDP 75 mg/m2 + 5FU 750 mg/m2 x 5 d (TTP 5.6mo, OS 9.2mo, 2yOS 18%, OR 37%, adverse events 69%) vs CDDP 100 mg/m2 + 5FU 1 g/m2 x 5 d (TTP 3.7mo, OS 8.6mo, 2yOS 9%, OR 25%, adverse events 59%).

JA Ajani et al (JCO 2007; 25:3205-9). V325 study. N=445. Randomized: TXT 75 mg/m2 + 5FU 750 mg/m2 civi x 5d + CDDP 75 mg/m2 (MST 6.1 mo, HR=1.38) vs 5FU 1 g/m2 x 5 civi + CDDP 100 mg/m2 (MST 4.8 mo). In addition there was improvement of QOL, TTP & OS.

A Roth et al SAAK (JCO 2007;25:3217-23). N=121. Randomized: EPI 50 mg/M2 + CDDP 60 mg/m2 + 5FU 200 mg/m2 d 1-21 (ORR 25%, MOS 8.3 mo), vs TXT 75 mg/m2 + CDDP 75 mg/m2 (ORR 18.5%, MOS 11 mo), vs TXT + CDDP + 5FU 300 mg/m2 civi d 1-14 (ORR 36.6%, MOS 10.4 mo).

SE Al-Batran et al (JCO 2008;26:1435-42). Gatroesophageal & gastric adenocarcinoma. N=220, median age 64 yo. Randomized: (FLO) 5FU 2.6 g/m2 24 h civi + FA 200 mg/m2 + LOHP 85 mg/m2 (PFS 5.8 mo, MST 10.7 mo, less toxicity hematological, N&V, alopecia, renal, TPE) vs 5FU 2 g/m2 24 h civi + FA 200 mg/m23 wkly + CDDP 50 mg/m2 (PFS 3.9 mo, MST 8.8 mo, less neuropathy). Age > 65 yo OR 41.3% vs 16.7%; TTF 5.4 mo vs 2.3 mo; PFS 6 vs 3.1 mo; OS 13.9 mo vs 7.2 mo, all favouring FLO. New standard.

J Ajani et al (Cancer 2008;113:945-55). Modification of TXT 40 mg/m2 + CDDP 40 mg/m2 + 5FU 2 g/m2 24 h civi q 2 wks vs CDDP + 5FU (OR 81% vs 57%).Other possibilities include: LOHP for CDDP, XEL for 5FU, TXT + CPT, EPI+LOHP+5FU, and S-1+BV.