5fluorouracil 375 mg/m^2 days 1–5 and leucovorin 20 mg/m^2 days 1–5 every 28 days.
The trial was powered ($\alpha = 5\%$, $1\text{-}\beta = 90\%$) to detect a 15% increase in 5-year survival (250 events required).
Of the 400 patients 3 were excluded because of positive margins. About 90% of patients in each arm were node positive (about 30% N3), and about 25% of the tumours were in the cardias. All the known prognostic factors were well balanced in the two arms.
Toxicity were mild in both arms mainly represented in PELFw arm by neutropenia and anaemia, while in the 5FU arm gastrointestinal toxicity was more common. At a median follow up of 3.5 years, the risk of death associated with PELFw was not statistically different (HR 0.89, 95%CI 0.65–1.23), such as the risk for progression (HR, 0.94, 95%CI 0.71–1.24) although it should be remembered that it is a comparison with another treatment arm. Surprisingly, in spite of the poor prognosis of these patients we did not observe a sufficient number of events (150 instead of 250). A final analysis with a median follow up of 54 months will be presented at the meeting.

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Similar safety results of capecitabine/cisplatin (XP) vs. continuous infusion of 5-FU/cisplatin (FP) from a phase III trial in patients (pts) with previously untreated advanced gastric cancer (AGC)

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Background: Combination of continuous infusion of 5-FU and bolus i.v. cisplatin is considered one of the standard chemotherapy regimens in AGC. Capecitabine is an oral fluoropyrimidine with proven efficacy and favourable safety in colorectal cancer, whose administration does not require hospitalisation or placement of central i.v. line. A phase II study of XP in pts with previously untreated AGC suggested that this combination would be comparable to FP in terms of efficacy with the known safety advantages of capecitabine over 5-FU. Efficacy data were as follows: overall response rate 55% (95% CI, 40–70%), median time to progression 5.8 months, and median overall survival 9.7 months [Kim et al. 2002]. A confirmatory phase III non-inferiority study was designed.
Materials and methods: Pts with previously untreated AGC were randomly assigned to: oral capecitabine (1000 mg/m^2 twice daily, days 1–14) and cisplatin (80 mg/m^2 i.v., day 1) every 3 weeks (XP arm), or to 5-FU (800 mg/m^2/day by continuous infusion, days 1–5) and cisplatin (80 mg/m^2 i.v., day 1) every 3 weeks (FP arm). Pts were treated until disease progression or unacceptable toxicities.

	% of pts with adverse events			
	XP (n = 108)		FP (n = 102)	
	All grades	Grade 3/4	All grades	Grade 3/4
Nausea/vomiting	64	5	71	7
Anorexia	25	2	25	0
Fatigue/asthenia	20	<1	25	2
Neutropenia	25	13	16	9
Stomatitis	12	3	29	7
Diarrhoea	14	3	14	3
Leukopenia	12	2	11	0
Hand–foot syndrome	17	<1	4	0
Dizziness	4	0	12	0
Thrombocytopenia	5	3	0	0

Results: From April 2003 to January 2005, 316 pts were enrolled in 46 centres across 13 countries. This is an interim safety analysis of the first 225 pts enrolled. The arms were well balanced for the following: median age (years, range): XP (56, 31–74), FP (56, 23–73); Karnofsky performance status (%, range): XP (80, 70–100), FP (80, 70–100); and male/female (%): XP (68/32) FP (72/28). The median number of cycles was 4 for XP and 4 for FP. Median follow-up was 5.6 months for XP and 5.6 months for FP. The rate of the most common, related, clinical adverse events (>10% all grades) and related grade 3/4 AEs (>2%) are presented in the table. All-cause, 60-day mortality was 3% for XP and 2% for FP; treatment-related deaths were <1% for XP and 0% for FP.
Conclusions: In the AGC setting XP has a similar safety profile to FP. Early efficacy data are expected in 2006 after 220 events and if positive would suggest that XP will be an attractive therapy for AGC, given the patient preference for oral chemotherapy.
Study sponsored by Roche

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Docetaxel when added to cisplatin-5-fluorouracil improves survival and maintains quality-of-life for a longer period in advanced gastric cancer: Final results of a Phase III trial

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Background: This Phase III portion of a Phase II/III randomized trial compared docetaxel (Taxotere®; T), cisplatin (C), and 5-fluorouracil (F; TCF) with CF in gastric cancer.
Materials and methods: Chemotherapy-na¿ve patients with locally recurrent or metastatic gastric adenocarcinoma (including gastroesophageal junction) received TCF – T 75 mg/m^2 d (day) 1, C 75 mg/m^2 d1, F 750 mg/m^2/d continuous infusion (c.i.) d1–5 every (q) 3 weeks (w) – or CF – C 100 mg/m^2 d1, F 1000 mg/m^2/d c.i. d1–5 q4w. Biased-coin randomization was stratified for center, liver metastases, prior gastrectomy, 5% weight loss, and measurability. Endpoints included time to progression (TTP; primary endpoint), overall survival (OS), overall response rate (ORR), time to treatment failure (TTF) and safety. Quality of life (QoL) was assessed using EORTC QLQ-C30 and EuroQoL EQ-5D instruments. Clinical benefit was assessed by time to definitive worsening of Karnofsky performance status (KPS) by one category.
Results: Of 445 randomized and treated patients (6 patients untreated/arm), median age was 55 years, median KPS was 90 (64% $\geqslant$90), and 97% had metastatic cancer. All efficacy endpoints significantly favored TCF (Table 1). Regardless of relationship to treatment, some grade 3–4 adverse events (AEs) and hematologic abnormalities were increased with TCF (diarrhea, infection, neutropenia and neutropenic infection and/or febrile neutropenia) while others were more frequent with CF (stomatitis, anemia). Treatment discontinuation due to AE was similar between arms (27% TCF, 25% CF) as was nonmalignant death within 30 days of last infusion (7% TCF, 7% CF). Time to 5% definitive deterioration in global health status was longer with TCF (median 6.5 months [mo]) versus CF (median 4.2 mo; log-rank p = 0.0121). Time to definitive deterioration in KPS significantly favored TCF (median 6.1 mo) versus CF (median 4.8 mo; log-rank p = 0.0088).

Table 1: Efficacy Results

	TCF (n = 221)	CF (n = 224)	log-rank P-value
TTP, median (mo)	5.6	3.7	0.0004
Overall survival, median (mo)	9.2	8.6	0.0201
2-year survival (%)	18%	9%	–
Overall response rate (%)	37%	25%	0.0106*
TTF (mo)	4.0	3.4	0.0335**

*chi-square; **Wilcoxon test

Conclusions: Adding docetaxel to CF consistently yielded superior efficacy compared with CF, including longer survival. Although TCF was associated with some increase in toxicity versus CF, this is expected and manageable. In addition, TCF maintained QoL and KPS for a longer period. TCF offers a new option for the treatment of AGC.