

Randomized phase III trial of capecitabine/cisplatin (XP) vs. continuous infusion of 5-FU/cisplatin (FP) as first-line therapy in patients (pts) with advanced gastric cancer (AGC): efficacy and safety results

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BACKGROUND

The oral fluoropyrimidine capecitabine has proven efficacy and safety in colorectal and breast cancer. Phase II data in AGC suggested that XP would show comparable efficacy to a standard FP regimen, with potential safety and convenience advantages. This phase III study evaluated XP vs. FP in first-line AGC.

METHODS

Pts with previously untreated measurable AGC received either oral capecitabine (1000mg/m² bid d1-14) + cisplatin (80mg/m² i.v. d1) q3w (XP arm) or 5-FU (800mg/m²/d continuous infusion, d1-5) + cisplatin (80mg/m² i.v. d1) q3w (FP arm). XP requires 1 day per 3 weeks in hospital; FP requires 5 days. Pts were

treated until disease progression or unacceptable toxicity. Primary endpoint: non-inferiority (NI) in progression-free survival (PFS), defined as upper limit of 95% CI of hazard ratio (HR) <1.4 (first test) and <1.25 (second test).

RESULTS

From Apr 03 to Jan 05, 316 pts were enrolled in 46 centers/13 countries. Arms were well balanced: median age (years, range) XP (56, 26-74), FP (56, 22-73); median Karnofsky PS 80 (range 70-100) in both arms; male/female (%): XP (64/36) FP (69/31). Median no. of cycles was 5 (XP and FP). Median follow-up is 22.1 months. Primary endpoint was met: HR 0.81 (95% CI 0.63-1.04). XP was superior to FP in terms of overall response rate (ORR, RECIST). Efficacy is

presented in the table. Most common treatment-related grade 3/4 adverse events (XP vs. FP) were: neutropenia (16 vs. 19%), vomiting (7 vs. 9%), stomatitis (2 vs. 7%), diarrhea (5 vs. 5%), and anemia (5 vs. 3%). Other grade 3/4 events occurred in <5% of pts. The rate of all-grade hand-foot syndrome was low (22 vs. 4%).

CONCLUSIONS

XP showed highly significant non-inferiority for PFS and significant superiority for ORR vs. FP with similar safety. These findings suggest that capecitabine should become the fluoropyrimidine of choice for AGC, given the efficacy, reduced hospitalization time and simplified regimen. ▲

	XP (N=160)	95% CI	FP (N=156)	95% CI	P
ORR, %	41	33-49	29	22-37	0.03
Median PFS, months	5.6	4.9-7.3	5.0	4.2-6.3	0.0001* 0.003** 0.10***
Median overall survival, months	10.5	9.3-11.2	9.3	7.4-10.6	0.27

*p-value for test of HR vs. NI limit of 1.4; **similarly with NI limit of 1.25; ***superiority. Subgroup analyses confirmed robustness of efficacy data.