

Randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric (OG) cancer: The REAL 2 trial

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BACKGROUND

The aim was to establish the potential use of the third generation platinum compound, oxaliplatin (O) & the oral fluoropyrimidine capecitabine (X) in untreated patients (pts) with advanced OG cancer.

METHODS

After stratification for PS and extent of disease, pts with histologically confirmed adenocarcinoma, squamous or undifferentiated carcinoma of the oesophagus, oesophago-gastric junction or stomach were randomised, in a 2 x 2 design, to 1 of 4 regimens; epirubicin,

cisplatin, fluorouracil (ECF), EOF, ECX or EOX. Doses E 50 mg/m², C 60 mg/m² & O 130 mg/m² IV 3 weekly; F 200 mg/m² IV daily & X 625 mg/m² twice daily PO continuously; for 8 cycles. The primary endpoint was overall survival. With 1000 pts (250 per arm) the study had 80% power to demonstrate non-inferiority of X over F and also O over C if the upper limit of the HR 95% CI excluded 1.23 ($\alpha=0.05$) in the per protocol population. Analysis was performed using the logrank test and Cox regression analysis.

RESULTS

1002 pts were randomised from 61

centres. Demographics were balanced, 89% were PS 0-1, 77% metastatic, median age 63 (range 22-83), 81% were male and 40% gastric primaries. Histology: adenocarcinoma in 88% and 52% poorly differentiated. 11 pts were ineligible and 27 pts were withdrawn before treatment commenced. Median follow up was 17.1 months and 850 events have occurred.

CONCLUSIONS

Capecitabine may replace 5FU and Oxaliplatin may replace Cisplatin in triplet regimens used for the treatment of advanced OG cancer. ▲

OS RESULTS FOR NON-INFERIORITY (2X2 COMPARISONS) AND INDIVIDUAL REGIMENS

2x2 comparisons Per Protocol	1 year OS (95% CI)	Median OS	HR (95% CI)
5FU: ECF + EOF	39.4% (35.0-43.7)	9.6 mths	1
Capecitabine: ECX + EOX	44.6% (40.1-49.0)	10.9 mths	0.86 (0.75-0.99)*
Cisplatin: ECF + ECX	40.1% (35.7-44.4)	10.1 mths	1
Oxaliplatin: EOX + EOF	43.9% (39.4-48.4)	10.4 mths	0.92 (0.80-1.05)*
Regimens ITT			
ECF n=263	37.7% (31.8-43.6)	9.9 mths	1
EOF n=245	40.4% (34.2-46.5)	9.3 mths	0.95 (0.79-1.15)
ECX n=250	40.8% (34.7-46.9)	9.9 mths	0.92 (0.76-1.11)
EOX n=244	46.8% (40.4-52.9)	11.2 mths	0.80 (0.65-0.97) ‡

* The Upper limit of the 95% CI excludes 1.23 we can therefore conclude non-inferiority ‡ p=0.025 comparison with ECF. There were no significant differences in response rates comparing ECF to, EOF, ECX and EOX (41%, 42%, 46%, and 48% respectively); grade 3-4 non haematological toxicity 36%, 42%, 33% and 45%; and grade 3-4 neutropaenia 42%, 30% (p=0.008), 51% (p=0.043) and 28% (p=0.001) respectively.