Efficacy and safety findings from a randomized phase III study of capcitabine + oxaliplatin (XELOX) vs. infusional S-FU/folinic acid (FA) + oxaliplatin (FOLFOX-6) as first-line treatment for metastatic colorectal cancer (MCRC)


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STUDY RATIONALE

- Capcitabine (Capecitabine) and oxaliplatin (Proxozel) are standard chemotherapy agents used in the treatment of metastatic colorectal cancer (MCRC).

- Oxaliplatin (Proxozel) is a platinum-based drug that inhibits DNA synthesis and replication by forming adducts with DNA bases.

- Capecitabine is a fluoropyrimidine prodrug that is converted to 5-flourouracil (5-FU) in the liver, which is then transported to the tumor site for chemotherapy.

- The study was designed to compare the efficacy and safety of XELOX (Capecitabine + Oxaliplatin) vs. FOLFOX-6 (Infusional 5-FU/folinic acid + Oxaliplatin) as first-line treatment for MCRC.

- The study was randomized, double-blind, and placebo-controlled.

- Patients were followed for 18 months after randomization.

METHODS

- **Study design:** A randomized, multinational phase III trial to compare Capecitabine + Oxaliplatin (XELOX) vs. Infusional 5-FU/folinic acid + Oxaliplatin (FOLFOX-6) as first-line treatment for MCRC.

- **Recruitment:** Patients were recruited from 19 countries in North America, Europe, and Asia between May 2004 and May 2005.

- **Randomization:** Patients were randomly assigned to receive XELOX or FOLFOX-6 in a 1:1 ratio using a minimization method.

- **Inclusion criteria:** Patients with non-resectable advanced/MCRC, life expectancy >3 months, no prior treatment for metastatic disease.

- **Exclusion criteria:** Previous adjuvant chemotherapy, no previous adjuvant chemotherapy.

- **Dosage:** XELOX (Capecitabine 1000 mg/m² bid, Oxaliplatin 100 mg/m² 2-hour infusion) vs. FOLFOX-6 (5-FU 2000 mg/m² 2-hour infusion, folinic acid 200 mg/m² 2-hour infusion, Oxaliplatin 85 mg/m² 2-hour infusion).

Efficacy

- **Primary criterion:** Non-inferiority of XELOX vs. FOLFOX-6 in per protocol (PP) population on best response rates of XELOX versus FOLFOX-6 as first-line therapy in patients with MCRC.

- **Secondary efficacy analyses:**were performed on the ITT population.

- **Safety:** NCI-CTC version 3.0.

- **Quality of life:** With FACIT (chemotherapy convenience and satisfaction) questionnaires.

- **Relative dose intensity of oxaliplatin in both arms.

- **Non-inferiority of XELOX vs. FOLFOX-6 in terms of progression-free survival (PFS) as first-line therapy in patients with MCRC.

- **Non-inferiority of XELOX vs. FOLFOX-6 in terms of overall survival (OS) as first-line therapy in patients with MCRC.

- **Limit of 95% unilateral CI (16.2%) was above non-inferiority margin of 15%.

- **Relaxed difference between groups on response rates (PT) calculated by log-rank test: 3.5% (90% Cl: 0.81, 1.30) were non-significant.

- **Median PFS and OS are similar between XELOX and FOLFOX-6.

- **XELOX and FOLFOX-6 are both highly effective as first-line treatments for MCRC.

- **XELOX induced more hand-foot syndrome (but this did not reach significance, p=0.088), fever, and diarrhea and less WBC count neutropenia than FOLFOX-6.

- **Death or survival data between beginning of treatment and death (progression or death).**

- **Safety (NCI-CTC version 3.0).**

CLINICAL AND HEMATOLOGICAL ADVERSE EVENTS

- **Non-inferiority vs. FOLFOX-6 in terms of hematologic and non-hematologic adverse events as first-line treatment for MCRC.

- **Non-inferiority vs. FOLFOX-6 in terms of quality of life as a result of chemotherapy toxicity.

- **Non-inferiority vs. FOLFOX-6 in terms of quality of life vs. FOLFOX-6 in terms of quality of life.

- **Non-inferiority vs. FOLFOX-6 in terms of quality of life as a result of chemotherapy toxicity.

- **Non-inferiority vs. FOLFOX-6 in terms of quality of life as a result of chemotherapy toxicity.

REFERENCES


*Note: 1 cycle of XELOX = 3 weeks; 1 cycle of FOLFOX-6 = 2 weeks.*