Effective management of patients receiving XELOX: evaluation of the impact of dose modifications on outcome in patients from the NO16966, NO16967 and NO16968 trials

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BACKGROUND

XELOX is a chemotherapy regimen made up of oral capcitabine and oxaliplatin. The recommended schedule is capcitabine 1000 mg/m² on days 1–15 plus oxaliplatin 130 mg/m² on day 1 every 3 weeks.

XELOX has established efficacy in the first-line and second-line treatment of patients with metastatic colorectal cancer (MCRC), and as adjuvant therapy in patients with resected stage III colon cancer.

XELOX has a well-characterized tolerability profile, but regional differences in fluoropyrimidine-related toxicities were noted in a pooled analysis presented in 2008.1

Patients receiving XELOX in the US appear to develop more toxicity compared with those in Europe or Asia.2

Despite the availability of clear and effective dose-modification guidelines for managing patients experiencing fluoropyrimidine-related toxicities, many physicians in North America start patients on lower than recommended doses of capcitabine.

The effect of capcitabine dose modifications on the efficacy of XELOX was analyzed using data from three large randomized phase III studies: – NO16964 (XELOX as 1st-line treatment for MCRC); – NO16967 (XELOX as 2nd-line treatment for MCRC); – NO16968 (XELOX as adjuvant treatment for stage III colon cancer).

METHODOLOGY

NO16964, NO16967 and NO16968 protocols included standard dose schedules modifications for capcitabine, 5-FU and oxaliplatin for treatment-related adverse events.

Safety parameters included adverse events, deaths, laboratory parameters, exposure to trial medications, dose modifications and withdrawals.

In NO16964 and NO16968, Kaplan-Meier curves for PFS were developed for patients with or without capcitabine dose modifications to assess their effect on efficacy.

CONCLUSIONS

In patients treated with XELOX, capcitabine dose modifications do not adversely affect patient outcomes in either the metastatic or adjuvant setting.

These data should not be interpreted to mean that a lower capcitabine starting dose can be used without compromising efficacy, as this concept was not tested in these analyses.

When initiating treatment with XELOX, the recommended doses should be used, i.e. capcitabine 1500 mg/m² bid on days 1–12 with oxaliplatin 130 mg/m² on day 1 every 3 weeks.

Dose modifications, if required, can be used to manage treatment-related toxicity without compromising efficacy.

REFERENCES