Phase III Trial of 24 Weeks vs. 48 Weeks Capecitabine Adjuvant Chemotherapy for Patients with Stage III Colon Cancer: Final Results of JFMC37-0801.

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BACKGROUND

Colorectal cancer (CRC) is the second cause of cancer-related death in Japan. It remains unclear that the clinical benefit of adjuvant chemotherapy for 48 weeks (approximately 12 months) in stage III CRC compared with adjuvant chemotherapy for standard 24 weeks (approximately 6 months).

According to the ACCENT database, 88.6% of recurrences occur in stage II and III CRC prior to 3 years after surgery, and recurrence risk is considered to be highest between 12 months and 18 months after alteration. 8

Oral administration of capecitabine for 6 months is at least equivalent to 5-FU/LV disease free survival (DFS) and overall survival (OS) as adjuvant chemotherapy in patients with stage III colon cancer (S-AI-1).

No clinical trials which investigated the optimal duration of oral capecitabine have yet been implemented for adjuvant treatments.

Surgery alone and chemotherapy for 6 months showed the highest risk between 12 months and 18 months after surgery, and other oral 5-FU compounds were administered for 12 months did not show recurrence peak between 12 months and 18 months after surgery.

The aim of this study is to detect whether 1-year adjuvant chemotherapy with oral 5-FU (capecitabine) in colon cancer reduces the peak of recurrence between 12 months and 18 months and provides long-term OS benefit.

METHODS

Study design: An open-label randomized phase III trial (Figure 1). Objective: To demonstrate that oral administration of capecitabine for 12 months is superior to capecitabine for 6 months in terms of disease-free survival (DFS) in stage II (Dukes/C) colon cancer patients. Primary endpoint: Disease-free survival (DFS) Secondary endpoint: Relapse-free survival (RFS) Overall survival (OS) 2-year DFS Adverse events Statistical design: n=1,200, 0.5% DFS rate estimated within 65% in 6M group, and 67% in 12M group. Total sample size was calculated to be 1,200.

RESULTS

Enrollment was conducted from September 2006 to December 2009. 1,304 patients were randomly assigned, with well balanced to baseline characteristics. At the time of this final analysis, median follow-up was 60 months with 426 DFS events out of 1304 pts (6M: 654, 12M: 650).

Figure 1. JFMC37-0801 study design

The 3-year and 5-year DFS for the primary endpoint was 75.1%, 68.7% in the 12M arm and 70.0%, 65.3% in the 6M arm, respectively (p=0.098, HR=0.866, 95%CI: 0.717-1.046). (Figure 3)

The 5-year DFS was 74.1% in the 12M arm and 69.3% in the 6M arm (p=0.007, HR=0.808, 95%CI: 0.658-0.952). (Figure 4)

The 5-year OS was 87.6% in the 12M arm and 83.2% in the 6M arm (p=0.015, HR=0.730, 95%CI: 0.551-0.972). (Figure 5)

Complete rate of protocol treatment was 77.5% in 12M arm and 46.1% in 12M arm. (Table 2)

Dose reduction was required for 37.5% of patients in 6M arm and 48.1% in 12M arm. (Table 3).

DFS superiority in 12 months treatment of capecitabine adjuvant chemotherapy was not demonstrated in patients with stage IIIC colon cancer.

However, p-values of OS and RFS comparing 12 months treatment with 6 months treatment were less than 0.025.

With regard to the optimal duration of adjuvant chemotherapy in stage III colon cancer, further investigation was considered to be necessary.

REFERENCES

1. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2175677/


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