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Original Research

A randomised-controlled trial of 1-year adjuvant chemotherapy with oral tegafur–uracil versus surgery alone in stage II colon cancer: SACURA trial

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KEYWORDS
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Abstract ***Background:*** Efficacy of adjuvant chemotherapy in patients with stage II colon cancer is still controversial. The SACURA trial is a randomised-controlled study evaluating the superiority of 1-year adjuvant treatment with oral tegafur–uracil (UFT) to surgery alone for stage II colon cancer.

Methods: Patients were randomly assigned to the surgery-alone group or UFT group (UFT at 500–600 mg/day for 5 days, followed by 2-day rest, for 1 year). The primary end-point was disease-free survival (DFS). Target sample size was 2000, determined with one-sided alpha of 0.05, power of 0.9 and assumed hazard ratio (HR) 0.729.

Results: A total of 1982 patients (997 in the surgery-alone group and 985 in the UFT group) were analysed. Median follow-up was 69.5 months, median age was 66 years and for stage IIA/IIB/IIC, the distribution was 84%/13%/3%.

The 5-year DFS rate was 78.4% in the surgery-alone group and 80.2% in the UFT group. The HR for DFS was 0.91 (95% confidence interval [CI], 0.75–1.10; p = 0.31); superiority of UFT was not demonstrated. Approximately 9% of patients experienced second cancers, which consist 40.7% of the DFS events. The 5-year relapse-free and overall survival rates of the surgery-alone and UFT group were 84.6% and 87.2% (HR, 0.82; 95% CI, 0.65–1.04) and 94.3% and 94.5% (HR, 0.93; 95% CI, 0.66–1.31), respectively. Subgroup analysis failed to disclose superiority in prognosis of adding UFT to the patients with risk factors for recurrence.

Conclusions: Superiority of 1-year adjuvant UFT over surgery alone was not demonstrated in stage II colon cancer. Patients with risk factors for recurrence did not benefit from UFT.

Trial registration: ClinicalTrials. Gov. #NCT00392899.

1. Introduction

Colorectal cancer has been the most common cancer in Japan since 2015 [1]. Adjuvant chemotherapy is the internationally accepted standard of care with established efficacy for stage III colon cancer, but its usefulness for stage II disease remains controversial. No randomised-controlled trial (RCT) has focused on stage II colon cancer only [2]. Although two old meta-analyses have reported the survival benefit of adjuvant chemotherapy using 5-fluorouracil (FU) agents alone [3,4], other pooled analyses and a large population database review have concluded otherwise [2,5].

One reason for the lack of consistent evidence showing the efficacy of adjuvant chemotherapy for stage II colon cancer may be the favourable outcomes of these patients at baseline. The Japanese multicenter registry reported a recurrence rate of approximately 13% [6,7]. Given this good outcome, a large sample size is necessary to confirm any benefit of adjuvant chemotherapy over surgery alone. Another reason would be the heterogeneity of stage II. Large-scale database studies disclose that subpopulations of patients with stage II colon cancer have widely different prognosis [6–8].

The major western clinical guidelines [9–11] list T4 lesions, less than 12 examined lymph-nodes (LNs), bowel perforation and obstruction, lymphovascular involvement, poorly differentiated histology, perineural invasion and elevated carcinoembryonic antigen (CEA) as poor prognostic factors in stage II colon cancer and recommend adjuvant chemotherapy for patients with these 'high-risk' features. However, the benefit of adjuvant chemotherapy for those patients has not been confirmed [2].

We therefore conducted the SACURA trial (Surgical Adjuvant Chemotherapy with UFT for Curatively