Preliminary Short Communication

Clinical trial comparing UFT-PSK combination adjuvant therapy and surgery-alone for Stage II rectal cancer

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INTRODUCTION

Colorectal cancer is the third most common cancer and one of the most frequent causes of cancer-associated mortality worldwide¹⁾. Complete resection is essential for the cure of colorectal cancer. On the other hand, patients with stage II/III colorectal cancer often develop tumor recurrence even after complete curative resection.

For decades, in Japan, protein-bound polysaccharide K (PSK) has long been surmised to improve prognosis of colorectal cancers through modification of immunological mechanisms and inhibition of immunosuppressive molecules^{2, 3)}. Moreover, some reports showed that PSK and tegafur/uracil (UFT) for stage II and III colorectal cancer improves overall survival in an adjuvant setting^{4, 5)}. However, these findings were mostly obtained from retrospective studies, subgroup analysis, or meta-analysis of clinical trials. Prospective randomized trials, mostly implemented in Japan, have shown promising results with respect to the effect of adjuvant non-specific immu-

notherapy of PSK combined with several oral fluorinated pyrimidine chemotherapies⁶⁻⁹⁾. However, those effects were borderline positive, and definitive evidence had not yet been obtained. In this regard, the prospective validation study was warranted to re-evaluate those findings.

The present study was conducted to give an answer to this clinical question by evaluating the effectiveness of UFT-PSK combination immunochemotherapy as an adjuvant therapy in comparison to surgery-alone for stage II rectal cancers

PROTOCOL DIGEST OF THE STUDY

Purpose

The aim of the present study was to evaluate the clinical effectiveness of UFT-PSK combination as adjuvant therapy in comparison to surgery-alone for stage II rectal cancer

Resource

Individual patients' data of clinical trial was provided from the Japanese Foundation for Multidisciplinary Treatment of Cancer (JFMC).

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Study setting and protocol review

The study is a randomized Phase III clinical trial. The protocol was approved by the Protocol Review Committee of JFMC.

Endpoints

The primary endpoint is disease-free survival. The secondary endpoints are overall survival and the correlations between various clinico-pathological parameters and prognosis.

Eligibility criteria

Tumors are staged according to UICC version 6. Inclusion criteria are as follows: 1) Stage II, histological confirmed adenocarcinoma of the rectum. 2) Patients who underwent resection of a rectal cancer with D2 or more lymph node dissection. 3) pN0 4) Performance status: 0-2. 5) Patients without receiving pre-operative chemotherapy, radiation therapy for another carcinoma. 6) Patients who have adequate hematologic, liver, and coagulation profiles 7) Patients that was able to start chemotherapy within 8 weeks after the operation. 8) Patients who have given informed consent to participate in this clinical study.

The exclusion criteria are as follows: 1) Ingestion impossibility or digestive organs stricture. 2) Serious co-existing morbidities. 3) Active synchronous or metachronous malignant disease. 4) Pregnant or lactating women. 5) Not suitable for participating in the study for any other reason.

Treatment methods

Control group: surgery-alone

UFT-PSK group: UFT, administered orally 400 mg/m²/day thrice daily after meal for 5 days and followed by 2 days rest (one cycle) for one year after surgery. PSK, administered orally 3 g/day thrice daily after meal for one year after surgery.

Evaluations and statistical analyses

Primary analysis was based on the intention to treat population and safety analysis was based on the population whose patients were excluded if they did not receive adjuvant therapy in the UFT+PSK group. The difference in clinical and pathological characteristics between UFT+PSK and surgery alone was determined using Fisher's exact test or the χ^2 test. The DFS and OS curves were calculated using the Kaplan-Meier method, and were compared by the stratified log-rank test with stratification factors (location [Ra or Rb], pathological T stage [T3 or T4], age [< 65 years old or ≥ 65 years old]). A Cox proportional hazards model including the above stratification factors as explanatory variables was used to perform to estimate the hazard ratio and its 95% con-

fidence interval. The worst grade of the adverse events during the trial were summarized as proportions with 95% confidence intervals and compared using χ^2 test between two groups. A value of $P \leq 0.05$ was defined as being statistically significant. The SAS 9.4 software (SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses. This study was approved by the IRB of the Japanese Foundation for Multidisciplinary Treatment of Cancer.

Data analysis

Individual Patients' clinical and pathological data have already been collected and fixed. Detailed results of this trial data will be published elsewhere.

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Conflict of interest statement

None declared.

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