Three-Weekly S-1 Monotherapy as First-Line Treatment in Elderly Patients with Recurrent or Metastatic Gastric Cancer

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Background/Aims: Elderly patients with advanced gastric cancer (AGC) have generally been excluded from clinical trials, and there are few data available on the treatment of these patients. The efficacy of palliative S-1 monotherapy as a first-line treatment regimen for elderly patients has not been well elucidated. Methods: For this study, 25 AGC patients were enrolled between January 1, 2007 and March 31, 2009; 4 cases were recurrent AGC and 21 cases were metastatic AGC at the time of diagnosis. These patients received S-1 therapy at a dose of 40 mg/m² twice daily for 14 days every 3 weeks. All of the patients were older than 70 years. Results: The median follow-up duration, the median progression-free survival, and the overall survival time were 8.7 months (range, 4.9 to 12.5 months), 4.9 months (range, 3.5 to 6.3 months), and 10.8 months (range, 6.6 to 15.0 months), respectively. Grade 3/4 nonhematologic toxicities were rare. Grade 3/4 neutropenia was noted in two patients. The partial response rate was 21.7% and stable disease was observed in 34.8% of the patients. Two patients (8%) died due to chemotherapy-associated toxicity during treatment (septic shock/intracranial hemorrhage). Conclusions: Oral S-1 chemotherapy seems to be effective as a first-line treatment regimen for elderly patients with metastatic or recurrent AGC. However, elderly patients receiving S-1 treatment should undergo continuous toxicity monitoring, since they are highly susceptible to adverse effects. (Gut Liver 2010;4:503-507)

Key Words: S-1; Elderly; Gastric cancer

INTRODUCTION

Although the incidence and mortality rates of gastric cancer have been decreasing, gastric cancer is currently the second most common cancer after lung cancer.1 In Korea, gastric cancer is the most commonly occurring cancer, and it is also the second leading cause of cancer-related deaths after lung cancer.2 The incidence of gastric cancer increases rapidly in the sixth and seventh decades of life.3 Approximately 60% of all cancers occur in individuals aged ≥65 years, and this percentage is expected to increase with the aging of the population.4, 5 Palliation of symptoms is generally achieved by chemotherapy, which confers considerable benefit for the overall survival.6,7 Providing adequate health care for elderly people is becoming an increasingly important issue in industrialized nations. Large randomized clinical trials have generally not included elderly patients with advanced gastric cancer (AGC) and so the data on the treatment of these patients are limited. The prognostic value of age for patients with gastric cancer remains controversial.3 Only a few studies have administered chemotherapeutic regimens to elderly patients, although chemotherapy has been confirmed to improve the survival and quality of life in patients with AGC. There is currently no standard chemotherapeutic regimen for elderly patients. S-1 is a newly developed oral fluoropyrimidine, and this is composed of a mixture of tegafur, 5-chloro-2,4-dehydroxypyridine, and potassium oxonate in a molar ratio of 1:0.4:1.8 S-1 is an oral anticancer drug that has been shown to be well tolerable and effective for the treatment...
of many solid tumors. Although the toxicity of S-1 is known to be acceptable and manageable, the information on this with respect to elderly patients is limited. In addition, the S-1 regimen for 2-week treatment followed by 1-week rest showed to reduce the adverse events and increase patient compliance.9,10 We conducted a retrospective study on the safety and efficacy of three weekly oral S-1 mono-therapy as a first-line treatment regimen for elderly patients with metastatic AGC.

MATERIALS AND METHODS

1. Patient eligibility

From January 1, 2007 to March 31, 2009, 25 AGC patients were enrolled in this study. The inclusion criteria of our study included the diagnosis of metastatic or recurrent gastric adenocarcinoma that was confirmed by histological examination in patients aged ≥70 years. Patients with the presence of at least one measurable lesion were enrolled.

The patients who had undergone prior chemotherapy for metastatic disease were not enrolled. Patients with a poor performance status (Eastern Cooperative Oncology Group [ECOG] performance status ≥3) and the patients with poor renal and liver function were excluded in the present analysis. Patients who had undergone prior adjuvant chemotherapy were enrolled provided that the therapy had been completed more than 6 months prior to the development of metastatic disease. Four cases were recurrent AGC and 21 were metastatic AGC at the time of diagnosis.

2. Treatment schedule and dose modification

S-1 was administered orally twice daily according to the intermittent schedule (two weeks of treatment followed by a week rest period, every three weeks). The initial dose of S-1 was determined on the basis of the patient’s body surface area (40 mg/m²). The actual doses of S-1 according to the body surface area (BSA) were: BSA < 1.25 m², 40 mg twice a day; 1.25 m² ≤ BSA < 1.5 m², 50 mg twice a day; and 1.5 m² ≤ BSA, 60 mg twice a day. Chemotherapy was continued until disease progression or unacceptable toxicity, and it was discontinued if the patient refused further treatment. The intensity adjustments to the dose of the S-1 were recorded throughout treatment.

3. Response evaluation to treatment and the adverse effects

The baseline evaluation of each patient included a complete medical history, physical examination, a complete blood count, the serum chemistry and analysis of the computed tomography (CT) scans of the measurable or nonmeasurable lesions. Physical examination, blood counts and serum chemistry were carried out before each cycle of therapy. The CT scans of the measurable lesions were assessed at baseline and CT scans were repeated for every three cycles of treatment. The tumor responses were classified according to the guidelines of the Response Evaluation Criteria in Solid Tumors (RECIST). A complete response (CR) was defined as the disappearance of all clinical evidence of the tumor. A partial response (PR) was defined as a decrease (≥30%) in the sum of the longest diameter (LD) of the target lesions. The baseline sum LD served as a reference. The patients with a CR or PR did not undergo confirmatory CT scans after four weeks if the patients’ symptoms, physical examination or chest X-ray before the next chemotherapy cycle did not show evidence of disease progression. Progressive disease (PD) was defined as at least a 20% increase in the sum of the LDs of the target lesions or the appearance of new lesions. Stable disease (SD) was defined as a tumor response that did not meet the above criteria of CR, PR, or PD.

Progression free survival (PFS) and overall survival (OS) were analyzed using the Kaplan-Meier method. The date of administering S-1 was considered the starting date. The PFS was assessed by measuring the time interval from the start of the S-1 treatment until confirmation of disease progression or death as a result of any cause. The OS was determined by measuring the time interval from the beginning of the treatment to the date of death. We censored the patients who were alive or were lost during the follow-up in the data analysis. All the statistical analyses were conducted using SPSS version 12.0 statistical software (SPSS Inc., Chicago, IL, USA). Toxicity was evaluated before each treatment cycle according to the National Cancer Institute Common Toxicity Criteria, version 3.0.

RESULTS

1. Patient characteristics

We finally analyzed 25 patients. The median age was 77 years (range, 71-83). Only one patient received prior adjuvant chemotherapy (six cycles of 5-FU and Cisplatin). The distribution of the ECOG performance status was as follows: nine patients (36%) with a performance status of 2, 14 patients (56%) with a performance status of 1 and two patients (8%) with a performance status of 0. Table 1 shows the patients’ characteristics in detail.