Adjuvant and Neoadjuvant Chemotherapy in Gastric Cancer: A Review

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Introduction

In contrast to the negative reports from the Western world on the adjuvant chemotherapy of gastric cancer, many Japanese papers describe favorable results in limited subsets of the disease [1–3]. This beneficial outcome has led to the incorporation of adjuvant chemotherapy into routine multimodality therapy of locally advanced gastric cancer in Japan. Comparison of reports from Western countries and Japan might allow the pointing out of some differences in clinical stages of patients subjected to chemotherapy and in the selection of regimens. Reduced tumor burden, proper selection of patients, appropriate selection of drugs or regimens with enough dose intensity, and well-designed clinical protocol seem to be mandatory for the requisites of a successful adjuvant chemotherapy trial. In addition, a further improvement in the treatment results of advanced gastric cancer and establishment of the clinical significance of adjuvant chemotherapy require an alternate approach. The present paper deals with a brief review of adjuvant and neoadjuvant chemotherapy in gastric cancer and includes some discussion for future trials.

Treatment Results of Adjuvant Chemotherapy

Tables 1 and 2 summarize the main adjuvant chemotherapy regimens [4–24] in gastric cancer. Since the late 1950s, clinical trials of adjuvant chemotherapy started in the form of a phase III study (controlled randomized study). In

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the early days, triethylenethiophosphoramide (thio-TEPA) [4, 5], 5-fluoro-2-deoxyuridine (FUDR) [6], 5-fluorouracil (5FU) [7] or mitomycin C (MMC) [13–16] was employed as a single-drug regimen in the adjuvant setting. The former two drugs did not produce any survival benefit in the large scale clinical trials conducted in the United States [4–6] (Table 1).

5FU was proven to be active in the treatment of advanced gastrointestinal cancers and was used in the adjuvant setting with single or multidrug regimens (Table 2). Single 5FU administration did not reveal survival benefits in cases of curative resection, except for a temporary benefit in a small subset [7]. Conflicting results have been reported in terms of the combination chemotherapy with 5FU and Methyl-CCNU in the United States. The Gastrointestinal Tumor Study Group (GITSG) [8] reported a clinical benefit of combination chemotherapy with 5FU and Methyl-CCNU, although two other concurrent studies [Veterans Administration Surgical Oncology Group (VASOG) and Eastern Cooperative Oncology Group (ECOG)] [9, 10] reported no benefit in comparison with surgery alone. The regimens employed by the three groups were identical, although there was a difference in the selection of patients: GITSG selected curative cases as the subjects of chemotherapy, while the other two groups had no limitations. A combination of 5FU, vinblastin (VBL) and cyclophosphamide (CPM), or 5FU and 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) also showed no benefit [11, 12].