Introduction

MASAKI KITAJIMA, M.D., FACS, FRCS (hon)

Vice President, International University of Health and Welfare, and Director of IUHW Mita Hospital, Tokyo, Japan

There are currently 934,000 patients suffering from gastric cancer around the world. In Japan the incidence of colon and breast cancers has a tendency to increase as a result of Westernization in lifestyle. Notwithstanding this fact, in Japan the incidence of gastric cancer is still high, accounting for 107,726 deaths in 2005, a mortality rate that, when compared with figures for other cancers, is second only to that of lung cancer. Until quite recently, the therapeutic outcome for gastric cancer has not been at all satisfactory. This condition is prevalent throughout Asian countries, and Japan and South Korea are in a position to lead the way in gastric cancer treatment that can be applied throughout the world. S-1 (TS-1[®]) is an oral anti-cancer agent combining tegafur, gimeracil (CDHP), and oteracil potassium (Oxo). Since the approval of its application for gastric cancer in Japan in 1999, its outstanding therapeutic effect has brought a dramatic change in chemotherapy for gastric cancer and has contributed to significant development in treatment for this form of cancer. CDHP, a component of TS-1, competitively blocks the catabolism of 5-fluorouracil (5FU) by dihydropyrimidine dehydrogenase (DPD) and intensifies its anti-cancer effect by maintaining high concentrations of 5FU in the blood and tissues. Furthermore, Oxo combined with TS-1 reduces the toxicity of 5FU to the digestive organs, thus allowing this preparation to be administered orally for an extended period. Even with an oral administration route, an outstanding efficacy of 46.5% was reported in a phase II clinical trial in which TS-1 was administered alone. In 2007, the American Society of Clinical Oncology (ASCO) and ASCO-GI (symposium on gastrointestinal cancers) in particular reported evidence of the efficacy of TS-1 in three phase III clinical trials (JCOG9912, SPIRITS trial, and ACTS-GC), in all of which TS-1 was used to treat advanced gastric cancer or as adjuvant chemotherapy following surgery for gastric cancer. This evidence has had a significant

impact not only on clinicians but also on researchers in the United States and Europe.

Unfortunately, TS-1 has yet to be accepted as the international standard for chemotherapy for gastric cancer, but the FLAGS trial, in progress under Dr. J. Ajani at the M.D. Anderson Cancer Clinic in the United States, shows great promise. The efficacy of TS-1 has been established for adjuvant chemotherapy following gastric cancer surgery and has been our research target for the past several years. Evidence from our research is reflected in the Japanese Gastric Cancer Association gastric cancer treatment guidelines. In Korea, meanwhile, the application of TS-1 to gastric cancer was approved in 2003. Aggressive clinical trials are under way at the moment, and combined with new drugs such as oxaliplatin, it is being administered for advanced, recurrent gastric cancers. Data on TS-1 are gradually being accumulated, not only in Japan and Korea but also in Europe and the United States.

We invited Dr. Ajani to a Japan–Korea DIF meeting so that we could further our knowledge of chemotherapy for gastric cancer as it has been studied in Japan and Korea, with special reference to TS-1. In this issue of the journal, experts from the two countries describe the current status of chemotherapy for gastric cancer, with special emphasis on the results from trials conducted in Japan and Korea and introduced at the Japan–Korea DIF meeting.

Dr. Masakazu Fukushima led the presentation by describing the theoretical aspects of the action mechanism involved in the synergism of TS-1 and other agents such as CDDP, CPT-11 and taxane. Next, Dr. Mitsuru Sasako reviewed the current status of adjuvant chemotherapy conducted on patients who had undergone surgery for gastric cancer, and he described the standard therapy that currently is in use. From the clinicopathological point of view, Dr. Wataru Ichikawa introduced prognostic factors related to the clinical effects of TS-1-based chemotherapy, and Dr. Hyun

Cheol Chung described prognostic factors for anemia that have been recognized among Koreans who were treated with TS-1 therapy. For first-line therapy of advanced, recurrent gastric cancer, Dr. Yeul Hong Kim described the TS-1/taxane combination therapy that is being conducted in Korea, and Drs. Kang Yoon Koo and Hiroya Takiuchi reported on TS-1/oxaliplatin and TS-1/CPT-11 combination therapies, respectively. Dr. Narikazu Boku described the results of clinical trials for advanced recurrent gastric cancers by the Gastrointestinal Oncology Study Group of the Japan Clinical Oncology Group (GOSG/JCOG), and Dr. Wasaburo Koizumi presented details of a TS-1/CDDP combination trial. Dr. Atsushi Otsu concluded the session by reviewing chemotherapy for advanced recurrent gastric

cancers and presenting an overview for the future of chemotherapy for gastric cancer, including molecular-targeted therapy.

The thrust of this issue is to emphasize that TS-1 now constitutes a standard chemotherapy for gastric cancer, and to predict which patients may benefit from its combinations with newer anticancer agents. The findings may provide keys to therapies tailored to individual patients. One of the research themes is to clarify the roles of anti-neoplastic agents (including molecular-targeted drugs) at the stage where standard therapeutic modalities are established.

We are confident that the contents of this issue offer truly valuable information as a review of current gastric cancer chemotherapy.