Department of Internal Medicine
Division of Clinical Oncology/Hematology

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General Summary

The immediate goals of our clinical and basic research are to investigate basic and clinical aspects of malignant diseases and to try to improve outcomes for patients with solid tumors and hematological malignancies, leading to the ultimate goals of improving the natural history of malignant diseases. We have also been performing several clinical trials and basic research studies throughout 2012.

Research Activities

Leukemias

Many patients with previously untreated hematological disorders have been referred to our department. The disorders in 2012 included acute myeloid leukemia (AML), 8 cases; acute lymphoblastic leukemia (ALL), 11 cases; chronic myeloid leukemia (CML), 2 cases; and myelodysplastic syndrome (MDS), 6 cases. We have performed clinical trials as a member of the Japan Adult Leukemia Study Group (JALSG), which is a distinguished leukemia research group established more than 20 years ago in Japan for AML, ALL, and CML. The JALSG protocol studies performed in 2012 were as follows: AML/MDS–HR CS–7 study of newly diagnosed AML; refractory anemia with excess blasts II, all-case registration cohort study; CML–207 (phase III); AML–209–GS; AML209–KIT; and ALL–CS–12. We also participated in several cooperative group studies and pilot studies: Aged Double–7 (newly diagnosed AML in the elderly: phase II), VEGA (MDS: phase II), a study of nilotinib (refractory CML: phase I/II), and a study of dasatinib (refractory CML: phase I/II).

Lymphomas

In 2012 we registered 73 patients with newly diagnosed non–Hodgkin’s lymphoma and 2 patient with Hodgkin’s lymphoma. We have performed clinical trials as a member of the Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG). The registration of study JCOG0406 (newly diagnosed mantle cell lymphoma: phase II) was completed, and the study JCOG0601 (newly diagnosed low–risk advanced diffuse large B–cell lymphoma: phase II/III) is a still–active protocol study that began in 2007. A randomized phase II study in patients with high–risk diffuse large B–cell lymphoma is also

**Myeloma**

We registered 6 patients with newly diagnosed multiple myeloma in 2012. A novel agent, the proteasome inhibitor bortezomib, became available in 2007, and we have used it with or without dexamethasone to treat patients who have refractory myeloma. A randomized phase II study was started in 2010 (JCOG0904) to evaluate the efficacy of bortezomib + dexamethasone versus thalidomide + dexamethasone in patients with relapsed or refractory chemoresistant multiple myeloma.

**Hematopoietic stem cell transplantation**

To investigate and establish safer and more effective hematopoietic stem cell transplantation (HSCT), we have performed serial clinical studies examining umbilical cord blood transplantation with a bone marrow-nonablative procedure, a bone marrow-nonablative procedure using antithymic globulin, and mechanisms of graft-versus-host disease in HSCT.

**Solid tumors**

Many patients with solid cancers have been referred to our division from related divisions or departments from both inside and outside our hospital. Several of our studies seeking improved therapeutic outcomes are in progress throughout our university hospital with related divisions or departments. The combination of fluorouracil (5-FU), epirubicin, and cyclophosphamide (FEC100) with or without taxotere therapy is an adjuvant therapy for patients with breast cancer treated with curative surgery. FEC100 followed by taxotere is a preoperative combination chemotherapy for patients with locally advanced breast cancer, aiming at limiting the extent of surgery. Adramycin and taxotere followed by taxotere and trastuzumab is a first-line chemotherapy for patients with advanced, metastatic breast cancer. Since late 2008 we have been investigating a combined-modality therapy of radiation and chemotherapy with docetaxel, cisplatin, and 24 hours’ continuous infusion of 5-FU (DCF regimen) for patients with locally advanced esophageal cancer. The study has been completed, and an improved protocol was launched in 2010. A novel drug-development study with an orally decaying formulation of S-1 in patients with advanced gastric cancer was finished in 2011. A multicenter cooperative randomized phase II study was started in 2011 to compare S-1 + cisplatin, S-1 + leucovorin, and S-1 + leucovorin + oxaliplatin for patients with advanced and recurrent gastric cancer and was completed in 2012. Because trastuzumab is also active in patients with human epidermal growth factor receptor 2-positive gastric cancer, we
treat such patients with capecitabine + cisplatin (XP) + trastuzumab. Our first-line chemotherapies for patients with advanced colorectal cancer are folinic acid, fluorouracil, and oxaliplatin (FOLFOX) and folinic acid, 5-FU, and irinotecan (FOLFIRI). Since antibodies against vascular endothelial growth factor and against epidermal growth factor receptor became available in 2007 and 2008, respectively, combination therapies of these antibodies and FOLFOX or FOLFIRI have also been performed.

**Palliative care**
The mission of the palliative care team for cancer pain is to relieve patients’ pain and anxiety to support the fight against cancer. Our team encourages the use of narcotics and has improved the control of cancer pain. In our division, we aim to attain individual goals by sharing our thoughts and to contribute to the further growth of palliative care at The Jikei University Hospital.

**Basic research**
One of our important activities is translational research on solid cancers and hematological malignancies. Deep and durable remission in hematological malignancies is essential for longer survival and even cure. Exploring minimal residual disease can be useful for evaluating eradication of malignant cells. We are now preparing a minimal residual disease assay using bone marrow cells from patients treated for multiple myeloma by applying the real-time polymerase chain reaction. Our studies of cancer fatigue are focused on patients with malignant disease. We are also preparing a study protocol evaluating fatigue by examining saliva in patients with multiple myeloma and breast cancer. By detecting human herpes simplex virus 6 particles in saliva, it would be possible to evaluate the degree of fatigue. Drug-sensitivity testing, to determine which patients are sensitive to which agent, is also important for cancer chemotherapy.

We are examining the correlation between drug sensitivity and gene expression, such as excision repair cross complementation group 1 and TS, using tissue samples from patients undergoing preoperative chemotherapy with docetaxel, cisplatin, and 5-FU for operable, locally advanced esophageal cancer.

Some of above mentioned research results have recently been collected for presentation at scientific meetings, and further research is in progress.

**Publications**