Department of Internal Medicine
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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 2010.

Research Activities

Leukemias
Many patients with previously untreated hematological disorders have been referred to our department. The disorders in 2010 included acute myeloid leukemia (AML), 10 cases; acute lymphoblastic leukemia (ALL), 6 cases, chronic myeloid leukemia (CML), 8 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 2010 were as follows: the AML/MDS-HR CS-7 study for newly diagnosed AML; refractory anemia with excess blasts II, all-case registration cohort study; APL-204 (phase III); CML-207 (phase III); AML-209-GS; and AML209-KIT. We also participated in several cooperative group studies and performed pilot studies: Aged Double-7 (newly diagnosed AML in elderly patients: 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 2010 we registered 82 patients with newly diagnosed non-Hodgkin's lymphoma and 2 patients with Hodgkin's lymphoma. We have performed clinical trials as a member of the Lymphoma Study Group of the Japan Clinical Oncology Group. Pivotal protocol studies in 2010 were JCOG0406 (newly diagnosed mantle-cell lymphoma: phase II) and JCOG0601 (newly diagnosed low-risk, advanced, diffuse large B-cell lymphoma: phase II/III. A randomized phase II study in patients with high-risk, diffuse, large B-cell lymphoma has also been started (biweekly rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone [R-CHOP] ± cyclophosphamide, cytarabine, dexamethasone, etoposide, rituximab [CHASER] versus melphalan, cyclophosphamide, etoposide,

and dexamethasone [LEED]; JCOG0908). Other cooperative studies examined biweekly rituximab, etoposide, prednisone, vincristine, hydroxydaunorubicin (R-EPOCH: relapsed and refractory B-cell lymphoma: phase II) and pirarubicin, cyclophosphamide, vincristine, and prednisolone (THP-COP: newly diagnosed T-cell lymphoma: phase II). A study of enzastaurin (non-Hodgkin's lymphoma: phase III double-blind) has been completed. Enzastaurin is a novel drug targeting protein kinase Cβ which has been extensively studied throughout the world, including the United States, the European Union, and Japan.

Myeloma

We registered 8 patients with newly diagnosed multiple myeloma in 2010. 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 performed to compare the efficacy of bortezomib + dexamethasone with that of thalidomide + dexamethasone in patients with relapsed or refractory chemoresistant multiple myeloma (JCOG0904).

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 department 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, 500 mg/m^2; epirubicin, 100 mg/m^2; and cyclophosphamide, 500 mg/m^2 (FEC100) with or without taxotere 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. Doxorubicin and taxotere followed by taxotere and trastuzumab is a first-line chemotherapy for patients with advanced metastatic breast cancer. We have been investigating a combined-modality therapy of radiation and chemotherapy with docetaxel, cisplatin, and 24 hours' continuous infusion of fluorouracil (DCF regimen) for patients with locally advanced esophageal cancer since late 2008. The study has been completed, and an improved protocol was launched this year. A novel drug-development study with an orally decaying formulation of S-1 has been performed for patients with advanced gastric cancer. Our first-line chemotherapies for patients with advanced colorectal cancer are folinic acid, fluorouracil, and oxaliplatin (FOLFOX) and folinic acid, fluorouracil, and irinotecan (FOLFIRI). Because antibodies against vascular endotherial growth factor and epidermal growth factor receptor became available in 2007 and 2008, respectively, combination therapies of these antibodies with

FOLFOX or FOLFILI were also performed.

Palliative care

The mission of the Palliative Care Team for Cancer Pain Purposes is to relieve patients' pain and anxiety to support the fight against cancer. Our team encourages the use of narcotics and aims to improve the control of cancer pain. In our new 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. The structural differences between M protein produced by myeloma cells and that from monoclonal gammmopathy of undetermined significance have been examined, and the function of ATP-binding cassette transporters in cancer chemotherapy has been studied in collaboration with the Keio University Department of Pharmacy. Transfer of the MDR1 gene into hematopoietic stem cells is a potential method of chemoprotection in cancer chemotherapy. Basic research using $CD34^+$ cells enables us to try such a strategy. The growth and differentiation of $CD34^+$ cells into which the MDR1 gene has been transferred have been investigated *in vitro* in collaboration with the Keio University Department of Pharmacy, and the results have recently been published.

Publications

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