

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 improve outcomes for patients with hematological malignancies and solid tumors, 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 2009.

Research Activities

Leukemias

Many patients with previously untreated hematological disorder have been referred to our department. The disorders in 2009 included acute myeloid leukemia (AML), 8 cases; acute lymphoblastic leukemia (ALL), 6 cases, chronic myeloid leukemia (CML), 2 cases; and myelodysplastic syndrome (MDS), 7 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 2009 were as follows: AML/MDS-HR CS-7 study of newly diagnosed AML, refractory anemia with excess blasts II, all-case registration cohort study; AML-201 VLA4 study (prognosis evaluation study); AML-206 DNR assigned group (relapse and refractory AML: phase I); APL-204 (phase III); APL-205R (relapsed and refractory APL: phase II); and ALL-202 (phase III). We also performed several collaborative group studies and pilot studies: Aged Double-7 (newly diagnosed aged AML: phase II); VEGA (MDS: phase II); nilotinib (refractory CML: phase I/II); and dasatinib study (refractory CML: phase I/II).

Lymphomas

In 2009 we registered 48 patients with newly diagnosed non-Hodgkin's lymphoma (NHL) and 4 patients with Hodgkin's lymphoma (HL). We have performed clinical trials as a member of the Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG-LSG). Important protocol studies in 2009 were JCOG0211-DI (newly diagnosed natural killer/T lymphoma: phase I/II) and JCOG0203-MF (newly

diagnosed follicular lymphoma: phase III). Other cooperative studies examined biweekly rituximab, etoposide, prednisone, vincristine, hydroxydaunorubicin (R-EPOCH: relapsed and refractory B cell lymphoma: phase II); pirarubicin, cyclophosphamide, vincristine, and prednisolone (THP-COP: newly diagnosed T-cell lymphoma: phase II); and enzastaurin (NHL: phase III double-blind).

Enzastaurin is a novel drug targeting protein kinase $C\beta$ that 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 (MM) in 2009. Bortezomib, a novel proteasome inhibitor, became available in 2007, and we have used it with or without dexamethasone to treat patients who have refractory myeloma.

Hematopoietic stem cell transplantation

To investigate and establish safer and more effective hematopoietic stem cell transplantation, 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 the mechanisms of graft-versus-host disease in hematopoietic stem cell transplantation.

Solid tumors

Many patients with solid cancer have been referred to our department from related divisions or departments in our hospital and outside our hospital. Several of our studies are in progress throughout our university hospital with related divisions or departments, seeking improved therapeutic outcomes. 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. Adriamycin and taxotere followed by taxotere and trastuzumab is a first-line chemotherapy for patients with advanced metastatic breast cancer. The standard treatment for operable, locally advanced esophageal cancer has been altered, resulting in the use of chemoradiation therapy rather than surgical resection alone or the combination of resection and radiotherapy. We, therefore, 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 such patients since late 2008. For patients with advanced gastric cancer, a combination chemotherapy of S-1 and cisplatin has been performed. Our first-line chemotherapies for patients with advanced colorectal cancer are folinic acid, 5-FU, and oxaliplatin (FOLFOX) and folinic acid, 5-FU, and irinotecan (FOLFIRI). Because antibodies against vascular endothelial growth factor and epidermal growth factor receptor became available in 2007 and 2008, respectively, combination therapies with these antibodies and FOLFOX or FOLFIRI 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 has been better able to control 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 hematological malignancies and solid cancers. The structural differences between M protein produced by myeloma cells and that from monoclonal gammopathy 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. We examined the conditions required for home death analysis of 9 outpatients who received chemotherapy.

Publications

Ichiba T, Kobayashi T, Inoue D, Arakawa Y, Sakuyama T, Aiba K. Conditions required for home death—analysis of nine outpatients received chemotherapy (in Japanese). *Gan To Kagaku Ryoho* 2009; **36 Suppl 1**: 39–41.

Yahagi Y, Usui N, Yamaguchi Y, Dobashi N, Yano S, Takei Y, Sugiyama K, Takahara S, Saito T, Minami J, Kobayashi T, Kamiyama Y, Morikawa T, Aiba K. Fractionated administration of gemtuzumab ozogamicin for refractory acute myeloid leukemia (in Japanese). *Rinsho Ketsueki* 2009; **50**: 1601–6.

Okawa Y, Aiba K. Molecular-targeted drugs. 1) Indications and the application of molecular-targeted drugs in hematological diseases. *Nippon Naika Gakkai Zasshi (in Japanese)* 2009; **98**: 1908–17.

Arakawa Y, Saito S, Yamada H, Aiba K. Simultaneous treatment with camptothecin and val-

proic acid suppresses induction of Bcl-X(L) and promotes apoptosis of MCF-7 breast cancer cells. *Apoptosis* 2009; **14**: 1076–85.

Yamaguchi Y, Usui N, Dobashi N, Yano S, Yahagi Y, Takei Y, Sugiyama K, Ogasawara Y, Saito T, Minami J, Kobayashi T, Katsube A, Kamiyama Y, Machishima T, Morikawa N, Otsubo H, Kaito K, Asai O, Aiba K. Gemtuzumab ozogamicin (GO) in relapsed/refractory patients with acute myeloid leukemia (in Japanese). *Gan To Kagaku Ryoho* 2009; **36**: 1105–9.

Yano S, Usui N, Dobashi N, Yahagi Y, Takahara S, Sugiyama K, Ogasawara Y, Saito T, Minami J, Kobayashi T, Nikaide T, Takeuchi K, Aiba K. A case of primary esophageal mucosa-associated lymphoid tissue lymphoma with a numerical abnormality of 18q21 detected by fluorescence in situ hybridization. *Ann Hematol* 2009; **88**: 703–4.