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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 successfully throughout 2015.

Research Activities

Leukemias

Many patients with previously untreated hematological disorders have been referred to our department. The disorders in 2015 included acute myeloid leukemia (AML), 26 cases; acute lymphoblastic leukemia (ALL), 9 cases; and chronic myeloid leukemia (CML), 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 clinical research and treatment of AML, ALL, and CML. The JALSG protocol studies performed in 2015 were as follows: JALSG-AML209-GS, JALSG-CBF AML209-KIT, JALSG-ALL-CS-12, JALSG-CS-11, JALSG-CML212, phaseIIJALSG-APL212, JALSG-APL212G, JALSG MDS212 (MDS212), JALSG-Ph(-) B-ALL213, JALSG Burkitt-ALL213, and JALSG Ph^{+}ALL213. 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 2015 we registered 81 patients with newly diagnosed non-Hodgkin's lymphoma. We have performed clinical trials as a member of the Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG). The study JCOG0601 (newly diagnosed, low-risk, advanced, diffuse, large B-cell lymphoma: phase II/III) was a pivotal protocol study beginning in 2007. 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 [bi-R-CHOP] ± cyclophosphamide, cytarabine, dexamethasone, etoposide, and rituximab [CHASER] vs 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).

Myeloma

We registered 11 patients with newly diagnosed multiple myeloma in 2015. 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. A randomized phase II study evaluating melphalan + predonisolone + bortezomib (MPB) induction chemotherapy for elder patients and patients who refuse stem-cell transplantation was started in 2015 in patients with multiple myeloma (JCOG1105).

In-house protocols are also under investigation. These investigations include a phase II study of the cyclophosphamide + bortezomib + dexamethasone (CVD) regimen for patients with newly diagnosed multiple myeloma and a phase II study of the cyclophosphamide + lenalidomide + dexamethasone (CRD) regimen for patients with relapsed and refractory multiple 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 mechanisms of graft-versus-host disease in hematopoietic stem-cell transplantation.

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. Since late 2008 we have been investigating a combined-modality therapy of radiation and chemotherapy with docetaxel, cisplatin, and 24 hours' continuous infusion of fluorourcil (5-FU) (DCF regimen) for patients with locally advanced esophageal cancer. The study has been completed, and the results have recently been published. Successively an improved protocol was launched 3 years ago and is now being investigated. In collaboration with another department we have performed and completed a novel drug-development study of an orally decaying formulation of S-1 in patients with advanced gastric cancer; the new formulation of S-1 has now become available for daily practice. 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). Because antibodies against vascular endothelial growth factor (VEGF) and against epidermal growth factor receptor (EGFR) became available in 2007

and 2008, respectively, combination therapies of these antibodies and FOLFOX or FOLFILI have also been performed. Because oral drugs are more convenient and safer, 5-FU is replaced by S-1 or capecitabine in such intravenous combination chemotherapy regimens as FOLFOX or FOLFILI, leading to the development of improved regimens of S-1 + oxaliplatin (SOX), capecitabine + oxaliplatin (XELOX), irinotecan + S-1 (IRIS), and capecitabine + irinotecan (XELIRI). Salvage therapies using regorafenib or trifluridine/tipiracil (TAS-102) became standard care for resistant and refractory advanced colorectal cancer.

Basic research

One of our important activities is translational research on solid cancers and hematological malignancies. We have been investigating an improved method enabling minimal residual disease to be detected in patients with multiple myeloma. Because the clinical requirement is urgent, persistent research is warranted. Cancer fatigue is now an emerging issue for patients with advanced malignant disease. We have been evaluating the correlation between cancer fatigue and human herpesvirus 6 reactivation using patient's salivary juice and blood samples, in collaboration with the Department of Virology. The preliminary results were reported at the annual meeting of the Multinational Association of Supportive Care in Cancer in Miami, Florida (USA). Gene expression analysis has been examined in blood samples to clarify efficacy and adverse effects in patients who have esophageal cancer and are undergoing chemoradiotherapy. Because esophageal cancer is a severe, life-threatening disease, such a study would be of great consequence. Supportive care in cancer is also important for patients with malignant disease and has been studied by us for many years. Measurement of the urinary level of liver-type fatty acid binding protein (L-FABP) can be used to predict renal damage caused by cisplatin. Therefore, we have been attempting to determine whether the L-FABP level should be measured for the early detection of renal damage in patients undergoing cisplatin combination chemotherapy, such as DCF and gemcitabine + dexamethasone + cisplatin (GDP). The studies are vigorously in progress.

Publications

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